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RADIOLOGY

A MONTHLY JOURNAL DEVOTED TO CLINICAL RADIOLOGY AND ALLIED SCIENCES

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Detroit, Michigan



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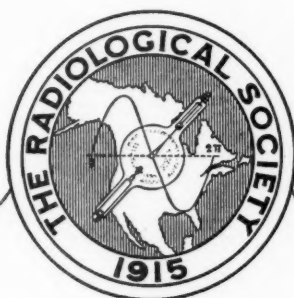
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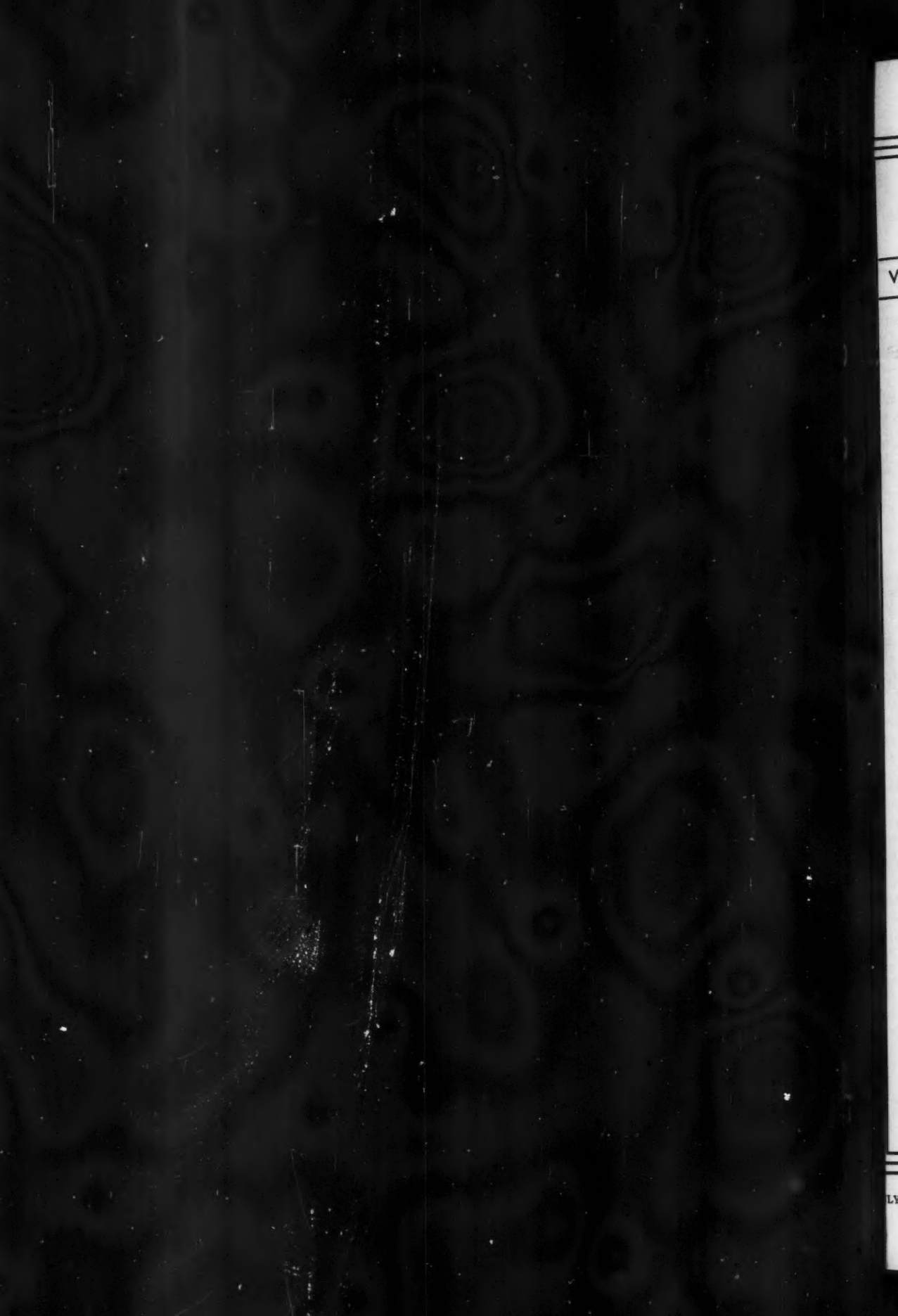
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Bone-Marrow Dose Produced by Radioactive Isotopes¹

EDWARD HOLODNY, B.S., HEATHER LECHTMAN, B.A., and JOHN S. LAUGHLIN, Ph.D.

THIS REPORT describes the design and construction features of a realistic phantom and dose-measuring system which make feasible experimental determination of the radiation dose distribution throughout the body, produced by internally located radioactive isotopes. The application of this system to the determination of the bone-marrow dose throughout the skeleton, from radium applicators in the cervix, is also presented. The method is being employed to ascertain the bone-marrow and other critical organ doses produced by a variety of radioactive isotopes either mechanically or metabolically located in the body.

When radiation is used therapeutically, the maximum absorbed tissue dose can be produced in the "target volume," with proper care and adequate technological facilities. Other healthy body tissues, however, are usually unavoidably irradiated during the course of treatment. This is particularly true when gamma-ray-emitting isotopes are employed internally. In such instances, where there is appreciable post-therapy survival, the possibility of radiation-induced disease may exist. The precise relationship between dose and biological effect for this outcome has not been established, nor have the relevant tissues involved been exclusively defined.

An example of this situation is the demonstration of increased incidence of leukemia in patients irradiated for ankylosing spondylitis. An analysis of these cases by Court-Brown and Doll (1) did not establish the dose-effect relationship (whether it be linear, threshold, or more complex in character) between the radiation and the disease. It is generally assumed, however, that in the case of radiation-induced leukemia, exposure of the bone marrow is important. Whether or not irradiation of other organs is also important is not known, and whether it is the average, the maximum, or some particularly localized dose which is significant is undetermined. Nevertheless, if one is able to ascertain the dose throughout the skeleton for a given irradiation procedure, corresponding dosages to other portions of the body, if those should prove to be of clinical significance, can be obtained later by interpolation and by suitable phantom measurements.

Determination of the absorbed dose produced in bone marrow by several radium cervix applicator arrangements is described here. The bone-marrow dose from radioactive seed implants (radon, iridium 192, cobalt 60, etc.) and by various internal distributions of iodine 131, gold 198, chromium 51, phosphorus 32, etc., will be the

¹From the Departments of Physics and Biophysics, Memorial Sloan-Kettering Cancer Center, New York, N. Y. Presented at the Forty-sixth Annual Meeting of the Radiological Society of North America, Cincinnati, Ohio, Dec. 4-9, 1960.

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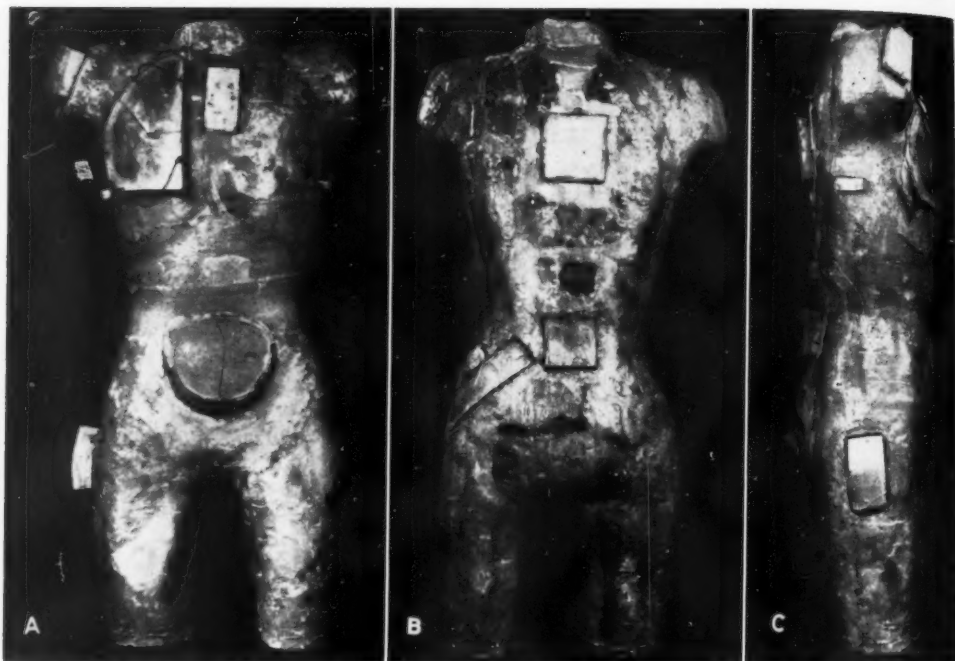


Fig. 1. Radioactive isotope phantom. A. Front view with chamber drawers partly out. B. Back view with chamber drawers in place. C. Side view with chamber drawers partly out.

subject of subsequent reports. The dose measurements were made in a realistic adult female phantom at representative sites throughout the skeleton. They include not only the maximum marrow-absorbed dose, but also its distribution, and have been further analyzed to indicate the mean marrow-absorbed dose and the integral marrow-absorbed dose. The marrow was chosen as the tissue of interest not because it is necessarily the most important or only important tissue, but because it is believed to have some relevance to the latent radiation induction of such diseases as leukemia. Furthermore, its geometrical distribution is such that knowledge of its absorbed dose distribution permits deduction of the absorbed dose in other tissues.

EXPERIMENTAL METHOD AND MATERIALS

A. Radioactive-Isotope Phantom

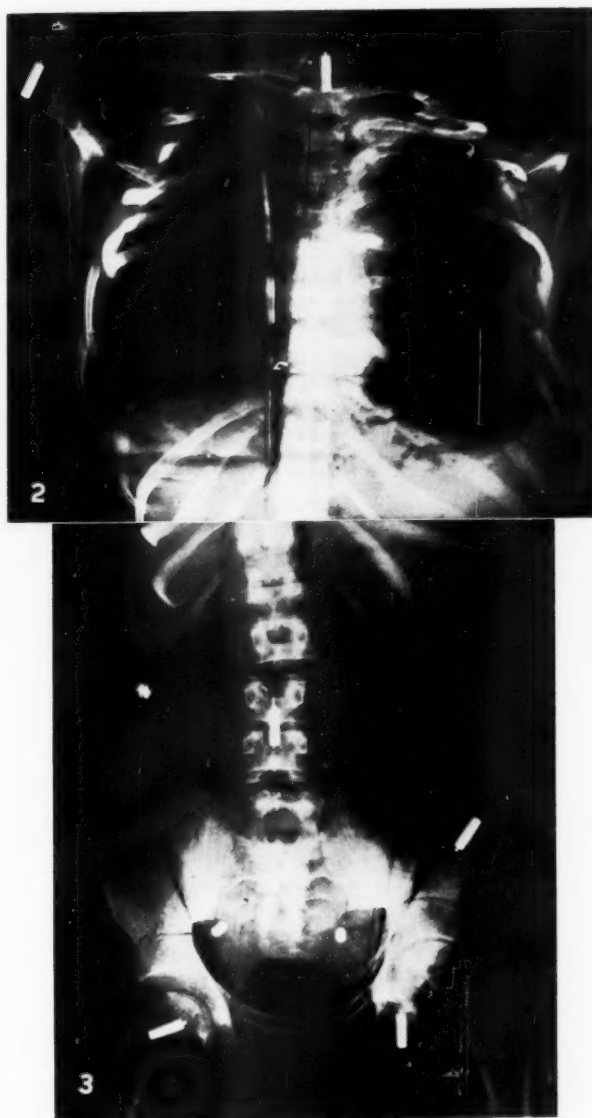
In order to measure directly the bone-marrow doses resulting from internally located radioactive isotopes, a phantom

man was constructed (Fig. 1). This was designed to simulate as closely as possible a human figure as to size, shape, density, and effective atomic number. The three primarily different forms of human tissue, muscle, lung, and bone, are represented by wax, cork, and an actual skeleton.

The bulk of the phantom consists of a mixture of beeswax and Mikrovan,² a commercial microcrystalline wax derived from petroleum. Its density is 0.94 gm./c.c., with an atomic number close to that of water. The lungs are of cork (0.3 gm./c.c.). Aside from the cork lungs and bone skeleton, the phantom is of solid wax. Since the air cavities which normally exist in the human body are not present in the phantom, the density of the wax was made slightly less than unity in order to correspond to the actual proportion of air and solid tissue.

The marrow cavities of the bones were filled with beeswax before their incorpora-

² Mikrovan is a product of Esso Standard Oil Company (formerly called Tervan).



Figs. 2 and 3. Radiographs of radioactive isotope phantom showing chamber positions.

tion in the phantom. The bones were boiled in wax, cooled, and withdrawn while the wax was still soft but no longer liquid. Several bones which were not to be used in the phantom were treated in this manner to determine whether or not a satisfactory degree of wax penetration of the marrow cavities would result. These

were radiographed after the wax had solidified, and no air spaces within the marrow cavities were evident on the films. They were then split in two, thereby exposing the marrow cavities, which were visually examined. The wax had entirely penetrated the cavities with no apparent intervening air spaces. Since this method



Fig. 4. Cervix drawer containing tandem and ovoids.

appeared satisfactory, all the bones used in the phantom were subsequently prepared in this manner.

A plaster cast of an existing Presdwood phantom (Laughlin *et al.*, 2) was used as a mold for a plaster cast into which the bones, cork, and wax were eventually placed. The cast was split into two sections, and the bones were assembled in their proper configurations within each section. They were secured in place as the liquid wax was poured into the mold and solidified around them. Templates of cross sections of a human figure were used to cut sheets of cork to the proper sizes so that, when stacked one upon another, they would approximate lungs in size and shape. The lungs were fitted inside the rib cage and secured with wax. Care was taken during this procedure to guard against any penetration of the cork by liquid wax. All remaining cavities were filled with wax heated just above the melting point so that, in cooling, contraction would be kept to a minimum. Any cracks produced by contraction of the cooling wax were immediately corrected.

The size of the resulting phantom is that

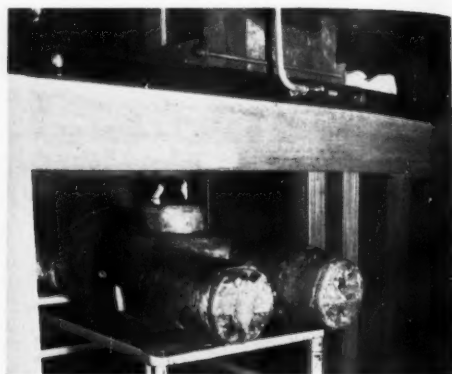


Fig. 5. Positioning of the cervix drawer in the pelvic cavity of the radioactive isotope phantom.

of a representative female adult. The spinal column from T-1 to L-5 is approximately 42 cm. in length; the width of the rib cage at the level of the sternum measures approximately 25 cm.; the transverse dimension of the pelvis (inside diameter) is 11 cm., while the distance from pubis to sacrum measures approximately 11 cm.

To determine the dose throughout the blood-forming regions of the marrow, provision had to be made for dose measurement at representative marrow sites. This was accomplished by drilling small holes in the interior of certain selected bones, in which miniature ionization chambers were placed. The chamber sites chosen included the sternum, thoracic vertebrae (T-1, T-7, T-12), lumbar vertebrae (L-3, L-4), two sections of rib, ilium, ischium, head of the femur, and head of the humerus (Figs. 2 and 3). In each case the section of the bone containing the chamber cavity together with some of its surrounding tissue was cut in the shape of a plug. Each plug of bone and wax was encased in a thin layer of Lucite so that a "drawer" construction resulted. Every "drawer" was made in such a way that it could be withdrawn from or inserted into the phantom with ease and was therefore readily accessible from the phantom exterior.

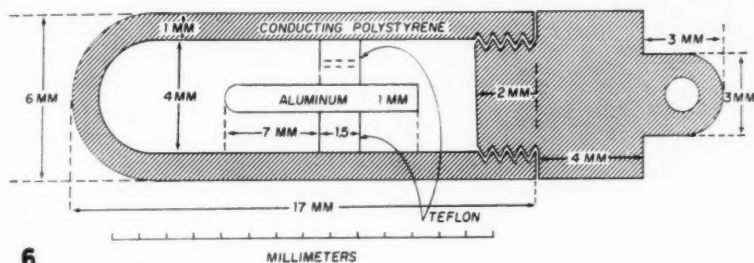
Chambers used in the arrangement described above measure the attenuation of the radiation as it traverses the body and

the bone, but do not measure the enhanced dose seen by that tissue immediately adjacent to bone. The dose measured is that experienced by a relatively large soft-tissue region inside the bone.

In order to place an actual Manchester tandem and ovoid cervix applicator inside the phantom in the proper anatomical position for treatment of carcinoma of the cervix, still another "drawer" had to be con-

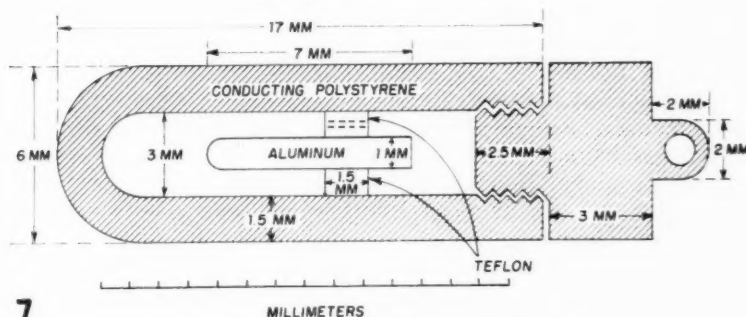
terior and lateral pelvic radiographs of the phantom with the drawer in place. When the desired position was achieved the Presdwood container was secured within the Lucite walls and the drawer was filled with wax. After the wax had solidified, the container with the applicator could be removed easily for loading and unloading (Fig. 5). Once the applicator was loaded, placed in the Presdwood con-

CHAMBER I



6

CHAMBER II



7

Fig. 6. High sensitivity gamma-ray chamber.

Fig. 7. Low sensitivity gamma-ray chamber.

structed (Fig. 4). A large cavity was made in the pelvic region of the phantom by scooping out the wax in that area. A drawer with thin Lucite walls was built, of exactly the same size and shape as the cavity, so that it could be fitted snugly into the space created for it. The tandem and ovoids were placed within a small Presdwood container, which in turn was placed inside the cervix drawer. The correct position of the applicator within the drawer was determined by obtaining anteropos-

terior and then in the cervix drawer, the entire unit could be dropped into or removed from the phantom at will.

B. Gamma-Ray Chambers

The miniature ionization chambers used in this experiment are of our own design (6). They were made of conducting polystyrene with an aluminum electrode insulated from the walls by a Teflon disk. A tiny hole was drilled in the Teflon to insure equalization of pressure in both

TABLE I: DOSE TO ACTIVE BONE MARROW (ROENTGENS)

Bone	3 Tube Tandem 2 Small Ovoids	87.5 mg.	2 Tube Tandem 2 Small Ovoids	75 mg.	2 Small Ovoids: 50 mg.	
	Dose Rate roentgens/hr.	Dose for 3,500-mg.-hr.	Dose Rate roentgens/hr.	Dose for 3,000 mg.-hr.	Dose Rate roentgens/hr.	Dose for 2,000 mg.-hr.
Measured Doses						
Ischium	6.67	267	6.84	274	5.60	224
Head of femur	5.80	232	5.84	234	4.36	174
Lumbar vertebrae L-3,4	3.96	158	2.75	110	1.48	59.2
Ilium	3.56	142	2.84	114	1.61	64.4
Thoracic vertebra T-12	0.48	19.2	0.38	15.2	0.22	8.8
Thoracic vertebra T-7	0.08	3.2	0.07	2.8	0.04	1.6
Sternum	0.06	2.4	0.05	2.0	0.03	1.2
Thoracic vertebra T-1	0.04	1.6	0.03	1.2	0.02	0.8
Head of humerus	0.03	1.2	0.03	1.2	0.02	0.8
Estimated Doses						
Sacrum	5	200	4	160	2.5	100
Ribs 9-12	0.48	19.2	0.38	15.2	0.22	8.8
Ribs 5-8	0.08	3.2	0.07	2.8	0.04	1.6
Ribs 1-4	0.04	1.6	0.03	1.2	0.02	0.8
Cervical vertebrae	0	0	0	0	0	0
Cranium and mandible	0	0	0	0	0	0

halves of the chamber. The chambers were made as small as possible so that they would fit easily into the marrow cavities of the bone. Small size was also desirable so that the measurements could be closely identified with specific points. The inside length of each chamber measured 15 mm., with an inside diameter of 4 mm. and a wall thickness of 1.0 mm. (Fig. 6). The response of the chambers to varying qualities of radiation was determined and, within the energy range of the gamma rays with which we were dealing, 0.2-2.2 Mev, their response was essentially constant.

The absolute sensitivity of the chambers was calibrated with gamma rays from a 25-mg. radium source of 1.2 cm. active length. The radium source was mounted on a thin Lucite rod approximately 13 cm. above the center of a round Lucite plate whose diameter measured 28 cm. The chambers were mounted on rods in a circle of 14 cm. radius and in such a way that the center of each was in the same plane as the center of the active portion of the source. Previous experiments had shown that it was necessary to mount both the source and the chambers at this distance above the Lucite plate in order to avoid scattering from the plate to the chambers. A large section of the plate itself was cut away in order to reduce the scattering to a mini-

mum. The entire assembly was supported by a Lucite rod 25 cm. above the floor. During the sensitivity measurements the chambers were charged to 300 volts and were exposed to the radiation for intervals of one hour. A Baldwin-Farmer electrometer was used to measure the amount of voltage discharge after this period. Each measurement was repeated five times, with results which agreed to within 1 per cent. The average sensitivity of a set of 7 chambers used in this experiment ranged from 120 to 132 volts/roentgen (Fig. 6), and the calibration of a set of lower sensitivity chambers constructed for higher dose rate regions ranged from 32.7 to 38.1 volts/roentgen (Fig. 7).

The response of the chambers was also found to be independent of dose rate over a range of 0.02 to 10.0 r/hr. During the course of the phantom experiment, the chambers were irradiated anywhere from three minutes to sixteen hours. No evidence of leakage was detectable over a twenty-four-hour period.

C. Experimental Procedure

In order to minimize radiation exposure to those conducting the experiment, a simple "remote control" system was devised for handling the cervix applicators, which contained between 50 and 87.5 mg. of radium. A diagram of the system is shown

in Figure 8. A rectangular hole was cut in one end of a table 6 feet long. The opening was of a size which just permitted the large cervix drawer to pass through it. The drawer was suspended over the opening by means of a rope that traveled over a single pulley to the other end of the table, where the operator could control its movement. A 6-inch thick lead wall completely surrounded the opening in the table top. The phantom rested on a lightweight cart under the table and could be easily and quickly positioned beneath the opening. A second lead wall was built under the table to shield the operator from the phantom. The phantom and the cervix drawer were thus hidden from the experimenter. To afford him a view of the drawer as he lowered it from its uppermost position inside the lead well to its final position within the phantom, a mirror was mounted at the side of the table. The drawer containing the radium applicator could be dropped into the phantom or removed from it within ten seconds or less.

The chambers were charged and fixed in their various positions within the bone cavities outside the radium exposure room. The phantom, with all its chamber drawers in place, was then quickly wheeled into position under the table and the cervix drawer was dropped into place. At the end of the exposure period the drawer was pulled up into the lead well above the table and the phantom was removed from the room. The chambers were then taken from their respective marrow cavities and their voltage discharge was measured.

EXPERIMENTAL RESULTS

Three different arrangements of the Manchester cervix applicator were used to determine bone-marrow doses produced by standard radium insertions. The first utilized a three-tube tandem (4.5 cm. active length, approximately 5.5 cm. total length) containing 3 radium tubes of 12.5 mg. each. The vaginal portion of the applicator consisted of two small ovoids (average diameter 2.25 cm.) separated by a washer (1 mm. separation). Each

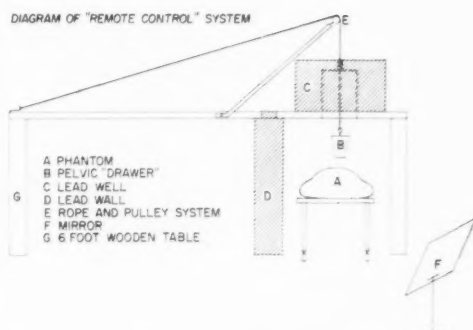


Fig. 8. Diagram of remote control operation of the radioactive isotope phantom.

ovoid contained a 25-mg. radium tube. The total activity of the applicator was 87.5 mg.

The second arrangement employed the same vaginal loading as the first, but a two-tube tandem with 25 mg. of radium replaced the longer uterine portion of the applicator previously used. The total activity of this second applicator was 75 mg. In the third set of measurements the uterine tandem was removed, and only the two small ovoids remained in place. This applicator contained 50 mg. of radium.

Table I lists the dose rates ($r/hr.$) at the various bone-marrow sites during each course of irradiation. It gives both the experimentally measured doses and the estimated doses to bones that did not contain ionization chambers or were not present in the phantom (e.g., cranium and mandible).

Not all of the bones containing active marrow in man were fitted with ionization chambers in the phantom, and it was necessary, therefore, to estimate the doses received by such bones during the course of irradiation. The marrow doses were first calculated by the inverse-square method, on the basis of the distances of such bones from the radium sources. It was immediately apparent that such calculated values were *much* higher than the doses *measured* in bones at similar distances from the applicators. A more accurate dose estimate for those bones lacking chambers was made by interpolation between the doses

TABLE II: DISTRIBUTION OF ACTIVE MARROW IN THE ADULT

Bone	Marrow Weight (5) (Gm.)	Fraction Red Marrow (8)	Active Marrow Weight (Gm.)	Distribution Active Marrow (%)
Ribs 1-4	57.4	0.4	22.9	2.2
Ribs 5-8	96.4	0.4	38.5	3.7
Ribs 9-12	53.0	0.4	21.2	2.0
Cranium and mandible	182.2	0.75	136.6	13.1
Scapulae; humeral heads and necks; clavicles	115.5	0.75	86.7	8.4
Sternum	39.0	0.6	23.4	2.2
Sacrum	194.0	0.75	145.6	13.9
Os coxae	310.6	0.75	233.0	22.3
Femoral heads and necks	53.0	0.75	40.0	3.8
Cervical vertebrae	47.4	0.75	35.8	3.4
Thoracic vertebrae T1-T4	46.1	0.75	34.5	3.3
Thoracic vertebrae T5-T8	63.3	0.75	47.6	4.5
Thoracic vertebrae T9-T12	87.6	0.75	65.8	6.3
Lumbar vertebrae	152.2	0.75	114.1	10.9
TOTAL	1497.7		1045.7	100.

which had been measured inside adjacent bones.

When the measurements reported here were made, the two chamber drawers located in the ribs were not yet complete. The dose to ribs 1-4 was therefore equated to the dose measured inside the first thoracic vertebra. Similarly, the dose to ribs 5-8 was equated to that measured at T-7, and the dose to ribs 9-12 to that measured at T-12.

Table I also gives the total dose in roentgens at each marrow site for a forty-hour exposure period. Since patients are often given two treatments of approximately forty hours each, the total marrow dose at each bone site in such cases would be double that shown in the table.

Estimation of Active Marrow Distribution: In an earlier report (4) on bone marrow exposure resulting from certain radiation diagnostic procedures, an active marrow distribution was assumed on the advice of several consulting hematologists and pathologists. Subsequently the work of Mechanik (5), published in 1926, was discovered in a search of the literature. The distribution of active marrow employed in this present study is based upon the total marrow weight and distribution measurements made by Mechanik (5, 6) on 13 cadavers, and upon modification of his figures on the basis of the observations of Custer (7) and of Custer and Ahlfeldt (8). Custer and Ahlfeldt measured the

proportions of active and inactive marrow in 100 persons and analyzed the changes in these proportions as a function of age. Their distributions indicate an absence of active marrow in the limbs of the adult, with the exception of the humeral and femoral heads. Evidence that this may result in an underestimate of the amount of active marrow in the skeleton is contained in the observations of Shillingford (9) who reported the presence of partial femoral activity in healthy adults (accident victims) and of high femoral activity in patients with heart disease. Turnbull (10) has reported high femoral activity in healthy adult females.

An average of the curves drawn by Custer and Ahlfeldt has been taken over the age range of twenty to forty years to obtain active marrow factors for each bone or group of bones. Table II gives the details of the marrow distributions. The first column lists the various bones of the skeleton; the second gives their total marrow weight in grams as measured by Mechanik; the third, based on the work of Custer and Ahlfeldt, indicates the fraction of active marrow contained in each bone or group of bones; the fourth lists the corresponding weights of active marrow in each of the indicated bones and is the product of columns 2 and 3; the fifth column shows the percentage of active marrow in each indicated bone as derived from the data in the rest of the table. This

TABLE III: ABSORBED ACTIVE MARROW DOSE (RADS)

Bone	3 Tube Tandem 2 Small Ovoids} 87.5 mg.		2 Tube Tandem 2 Small Ovoids} 75 mg.		2 Small Ovoids: 50 mg.	
	Dose for 3,500 mg.-hr. (roentgens)	Mean Active Marrow Dose (rads)	Dose for 3,000 mg.-hr. (roentgens)	Mean Active Marrow Dose (rads)	Dose for 2,000 mg.-hr. (roentgens)	Mean Active Marrow Dose (rads)
Ribs 1-4	1.6	0.03	1.2	0.02	0.8	0.01
Ribs 5-8	3.2	0.12	2.8	0.10	1.6	0.05
Ribs 9-12	19.2	0.38	15.2	0.30	8.8	0.17
Cranium and Mandible	0	0	0	0	0	0
Scapulae; humeral heads and necks; clavicles	1.2	0.09	1.2	0.09	0.8	0.06
Sternum	2.4	0.05	2.0	0.04	1.2	0.02
Sacrum	200	27.3	160	21.8	100	13.6
Os coxae	205	44.8	194	42.4	144	31.4
Femoral heads and necks	232	8.65	234	8.71	174	6.48
Cervical vertebrae	0	0	0	0	0	0
Thoracic vertebrae T-1-T-4	1.6	0.05	1.2	0.04	0.8	0.02
Thoracic vertebrae T-5-T-8	3.2	0.14	2.8	0.12	1.6	0.07
Thoracic vertebrae T-9-T-12	19.2	1.18	15.2	0.94	8.8	0.54
Lumbar vertebrae	158	16.9	110	11.7	59	6.3
TOTAL		99.7		86.3		58.7
	Integral active marrow dose (gm.-rads) = 1.042×10^5		Integral active marrow dose (gm.-rads) = 0.902×10^5		Integral active marrow dose (gm.-rads) = 0.614×10^5	

distribution is essentially the same as that used by the Adrian Committee (11). It is also, somewhat fortuitously, not very different from the estimated distribution used previously by us (2).

Analysis of Results: With the use of the values for the distribution of active marrow given in Table II, the mean active marrow dose received by the phantom was calculated for each of the three cervix applicator arrangements. This dose was obtained by multiplying the dose (in rads) to the marrow at a particular bone site by the percentage of active marrow at that site and then summing the weighted doses at all the sites. The resulting values, which are given in Table III, indicate the mean dose to the blood-forming portions of the marrow.

The mean integral marrow doses, also listed in Table III, were obtained through multiplication of the mean active marrow dose by the total number of grams of active marrow in the bone.

Points "A" and "B": When the phantom described above was being constructed,

two chamber positions were created in the pelvic region which correspond in anatomical position to points A and B, the two points of dosage control traditionally used in radium cervix therapy. Tod and Meredith (12) describe point A as being "... a point 2 cm. lateral to the center of the uterine canal and 2 cm. from the mucous membrane of the lateral fornix in the plane of the uterus..." Point B is located 5 cm. lateral to the center of the uterine canal and 2 cm. from the mucous membrane of the fornix. Since the phantom was undergoing precisely the same type of irradiation as might a patient with carcinoma of the cervix, it was deemed of interest to measure directly the doses received by points A and B under such radium treatment. Measurements were made with only the first of the three cervix applicators, that is, the arrangements consisting of a three-tube tandem and two small ovoids (87.5 mg.).

After the measurements were completed, a set of anteroposterior and lateral localization films of the pelvis were obtained with



Fig. 9. Radiograph of radioactive isotope phantom showing tandem and ovoids and the position of points A and B.

the applicator in place. Metal plugs replaced the chambers at points A and B so that the points would be visible on the roentgenograms (Fig. 9). At the same time, A and B were independently located on the films in the same manner as in patient dosimetry. The plotted points coincided exactly with the images of the metal plugs located at the chamber positions. We proceeded to calculate the doses to points A and B, using first the Holt nomographic wheel (13) and then the Memorial Physics Department isodose curves (series 0:1-3; T-1-0°; T-4, d-90°), two of the methods routinely used in patient dosimetry. These two calculation procedures are based on the geometrical decrease of intensity from point sources only (inverse-square law) and do not allow for absorption and scattering. Table IV compares the dose rates measured at A and B with those calculated at the two points.

TABLE IV: MEASURED AND CALCULATED DOSES AT POINTS A AND B

	Point A (r/hr.)	Point B (r/hr.)
Measured dose	75.9	25.0
Holt nomographic wheel	77.0	25.6
Isodose curves	72.0	23.0

The closeness of agreement of measured dose rates with those calculated is due to the small separation of points A and B and the active sources, in which case the effects of absorption and scatter are not important.

SUMMARY

The absorbed dose produced in active bone marrow by radium treatment of carcinoma of the cervix was measured in a wax and cork phantom containing a real skeleton and closely resembling the human body with respect to size, shape, density, and atomic number. Certain representative bones of the skeleton were fitted with miniature ionization chambers that measured the radiation dose produced by three arrangements of radium in cervix applicators of the Manchester type.

The mean absorbed active marrow dose produced by radiation from a cervix applicator containing 87.5 mg. of radium was found to be 99.7 rads in forty hours. The mean absorbed dose for the smallest applicator, which contained 50 mg. of radium, was 58.7 rads. The integral active marrow dose ranged from 1.04×10^5 gram-rads for the largest applicator to 0.61×10^5 gram-rads for the smallest. All exposures were forty hours each.

Measured doses at points A and B in the pelvis and doses calculated by conventional dosimetry methods showed a close correlation, attributable to the short distances between these points and the sources.

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REFERENCES

1. COURT-BROWN, W. M., AND DOLL, R.: Leukaemia and Aplastic Anaemia in Patients Irradiated for Ankylosing Spondylitis. Medical Research Council Special Report No. 295. London, Her Majesty's Stationery Office, 1957.

2. LAUGHLIN, J. S., MEURK, M. L., PULLMAN, I., AND SHERMAN, R. S.: Bones, Skin, and Gonadal Doses in Routine Diagnostic Procedures. *Am. J. Roentgenol.* **78**: 961-982, December 1957.
3. GARRETT, R., AND LAUGHLIN, J. S.: Memorial Laboratory Report. Not published.
4. EPP, E. R., WEISS, H., AND LAUGHLIN, J. S.: Measurements of Bone Marrow and Gonadal Dose from the Chest X-Ray Examination as a Function of Field Size, Field Alignment, Tube Kilovoltage, and Added Filtration. *Brit. J. Radiol.* **34**: 85-100, February 1961.
5. MECHANIK, N.: Untersuchungen über das Gewicht des Knochenmarkes des Menschen. *Ztschr. f. d. ges. Anat.* **70**: 58-99, 1926.
6. WOODARD, H. Q., AND HOLODNY, E.: A Summary of the Data of Mechanik on the Distribution of Human Bone Marrow. *Physics in Med. & Biol.* **5**: 57-59, July 1960.
7. CUSTER, R. P.: An Atlas of the Blood and Bone Marrow. Philadelphia, W. B. Saunders Co., 1949, p. 29.
8. CUSTER, R. P., AND AHLFELDT, F. E.: Studies

on the Structure and Function of Bone Marrow; Variations in Cellularity in Various Bones with Advancing Years of Life and Their Relative Response to Stimuli. *J. Lab. & Clin. Med.* **17**: 960-962, July 1932.

9. SHILLINGFORD, J. P.: The Red Bone Marrow in Heart Failure. *J. Clin. Path.* **3**: 24-39, February 1950.

10. TURNBULL, H. M.: Notes on Normal and Pathological Erythropoiesis. [In] *The Anaemias*, by J. M. Vaughan. New York and London, Oxford University Press, 1934.

11. ELLIS, R. E., AND HAMMOND, B.: British Estimate of the Mean Marrow Dose per Capita per Year from Diagnostic Radiology. London, Adrian Committee on Radiology Hazards to Patients, 1959. (Private communication)

12. TOD, M. C., AND MEREDITH, W. J.: Radium Dosage; The Manchester System. Edinburgh, E. & S. Livingstone, 1958.

13. HOLT, J. G.: A Nomographic Wheel for Three-Dimensional Localization of Radium Sources and Calculation of Dose Rate. *Am. J. Roentgenol.* **75**: 476-483, March 1956.

SUMMARIO IN INTERLINGUA

Doses in le Medulla Ossee, Producite per Isotopos Radioactive

Le dose absorbite in active medulla ossee como resultado de tractamento a radium de carcinoma del cervice esseva mesurate in un phantoma de cera e corco continente un ver skeleto e resimilante fortemente le corpore human con respecto a dimension, conformation, densitate, e numero atomic. Certe representative ossos del skeleto esseva equipate con miniaturisate cameras de ionisation que mesurava le dose de radiation producite per tres differente arrangiamentos de applicatores de radium al cervice, typo Manchester.

Esseva trovate que le valor medie del dose absorbite in medulla active como re-

sultato de radiation ab un applicator cervical continente 87,5 mg de radium esseva 99,7 rad in quaranta horas. Le valor medie del dose absorbite in le caso del plus micre applicator (que contineva 50 mg de radium) esseva 58,7 rad. Le dose integral al medulla active variava inter $1,04 \times 10^5$ gramma-rad pro le plus grande applicator e $0,61 \times 10^5$ gramma-rad pro le plus micre. Omne le expositiones durava quaranta horas.

Le doses mesurate in puncto A e puncto B in le pelve e le doses calculate pro ille punctos per medio del currente methodos dosimetric monstrava un alte correlation.

Plasma I¹³¹ Determination and Thyroidal I¹³¹ Uptake in the Diagnosis of Hyperthyroidism "Problem" Cases¹

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THIS IS A report of clinical experience with the use of 48-hour protein-bound plasma I¹³¹ assays (PBI¹³¹) and 24-hour thyroidal uptake measurements for the diagnosis of hyperthyroidism "problem" cases. PBI¹³¹ determinations were limited to patients with "equivocal" thyroidal uptakes (40 to 59 per cent at 24 hours) or with some clinical or laboratory inconsistency which made it desirable to obtain information in addition to the thyroid uptake. The primary purpose of this investigation was to evaluate the usefulness of 48-hour PBI¹³¹ determinations as supplemental data for these patients in whom the diagnosis or exclusion of thyrotoxicosis was *unusually difficult*. The results presented, therefore, are *not* an estimate of the uptake or PBI¹³¹ distribution in *all* patients referred for thyroid function study.

Instead of interpreting every test result as either "toxic" or "non-toxic," it should be possible on the basis of experience to derive a method for objectively estimating the probability that a given "problem" patient is thyrotoxic. Accordingly, a secondary purpose of this investigation was to determine the distribution of thyroidal uptake and PBI¹³¹ values in these cases in a manner that would permit quantitative estimation of the "probability" of thyrotoxicosis.

METHODS AND CASE MATERIAL

The measurement and standardization of the tracer doses of I¹³¹ and the counting arrangements used for the uptake determinations have been previously described (1). The expected standard deviation of the uptake measurements due to all

sources of physical error was estimated to be 10 to 12 per cent of the value for all tracer uptakes exceeding 10 per cent of the administered dose.

The total plasma I¹³¹ concentration was measured in a well-type scintillation counter. For the PBI¹³¹ studies done early in the series, the plasma proteins were precipitated with trichloroacetic acid. The precipitate was washed three times, redissolved in 4N sodium hydroxide and measured for I¹³¹ activity. In most cases, however, the PBI¹³¹ was separated from the total plasma I¹³¹ by the use of an ion-exchange resin.³ Approximately 1 gm. of resin was added to 6 or 7 ml. of plasma in a test tube and then "flurried" for five minutes with a motor-driven shaker. The resin was spun down with a centrifuge and 5 ml. of free plasma were transferred to another test tube for the PBI¹³¹ measurement. An investigation showed that both methods give essentially the same results (see Appendix A).

Within the accuracy of the measurement, the total plasma I¹³¹ (TPI¹³¹) must always be as high or higher than the PBI¹³¹. Therefore, as recommended by Newburger (2), TPI¹³¹ values less than 0.27 per cent of the administered dose per liter of plasma were considered to be decisive, and the plasma was not fractionated. Of 243 plasma values that were less than 0.27 per cent, 84 are PBI¹³¹ values and 159 are TPI¹³¹ values; all are hereafter referred to as PBI values.

Five hundred consecutive plasma I¹³¹ determinations were considered for this study. Of this number 142 were excluded: 22 because of a history of medication which might have altered thyroid function, 13

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³ Amberlite Xe-117 and Amberlite IRA-400 in chloride phase, manufactured by Rohm and Haas Co., Philadelphia, Penna.

TABLE I: CASE MATERIAL

	No Cardiac Disease	Angina Pectoris	Cardiac Decom- pensation	Angina and Decom- pensation	Totals
No thyroid enlargement					
Non-toxic	91	14	32	12	149
Toxic	24	..	12	4	40
Diffuse thyroid enlargement					
Non-toxic	32	1	4	2	39
Toxic	52	6	8	..	66
Single thyroid nodule					
Non-toxic	15	..	1	2	18
Toxic	11	..	6	..	17
Multiple thyroid nodules					
Non-toxic	11	2	5	2	20
Toxic	3	1	5	..	9
TOTALS	239	24	73	22	358

because the tracer dose exceeded 200 μ c or because of known technical error, 25 because the patients had thyroid cancer, 43 because the uptake was not measured within the range 24 ± 4 hours after administration of the tracer dose, and 39 because the blood sample was not drawn within the range 48 ± 6 hours. The study is thus based on 358 tracer procedures.

Each case was assigned a final diagnosis on the basis of all available information. This included a complete history, a physical examination, and for most patients laboratory studies such as basal metabolic rate, serum protein-bound iodine determinations, and serum cholesterol estimations. The final diagnosis was usually made in collaboration with the Endocrine Section of the Medical Clinic of the Hospital of the University of Pennsylvania. Since no patients were clinically hypothyroid, the final diagnosis was always either "thyrotoxic" or "not thyrotoxic," although in 4 cases the I^{131} uptakes were in the hypothyroid range.

In addition to the status of thyroid function, the following diagnostic information was coded for each patient: presence or absence of thyroid enlargement, palpable nodules in the thyroid, cardiac decompensation, or angina pectoris. Thyroid glands containing palpable nodules were always classified as enlarged. All patients receiving digitalis or other medication for cardiac decompensation were classified as decompensated, regardless of the degree

of success of the cardiac medical management. The distribution of the material according to these classifications is shown in Table I.

Any previous medical, surgical, or radiologic treatment of thyrotoxicosis was also coded. History of medications which might affect thyroidal physiology was carefully inquired for and recorded.

Finally, an attempt was made to mark, for separate analysis, those cases in which the diagnosis might have been determined by the plasma I^{131} value. This evaluation is necessarily subjective, but a rigorous effort was made to indicate every case in which it was thought even remotely possible that the final diagnosis might have been different if the PBI¹³¹ had not been known.

RESULTS

1. *Uptakes:* The 358 24-hour thyroidal uptake values were arranged in ascending numerical order and divided into ten groups of approximately equal number. The percentage of thyrotoxic patients in each group is shown by the vertical bars in Figure 1. The procession of these bars approximates a curve. This curve is of interest because it represents, for our case material, the likelihood of thyrotoxicosis as a function of the uptake value. If such a curve were known reliably for the population of patients referred or selected for thyroid function study in a given institution, it would be possible to

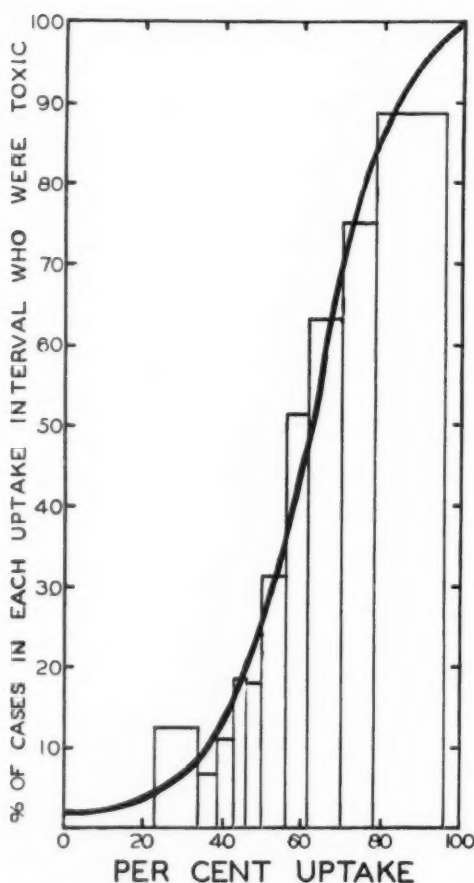


Fig. 1. Incidence of thyrotoxicosis versus 24-hour thyroidal uptake. Each vertical bar represents about 34 cases. In addition, there were 16 non-toxic cases with uptakes less than 23 per cent and 4 toxic cases with uptakes greater than 96 per cent. The curve is plotted from Equation [2] in the text.

predict for any given uptake the percentage of patients with that uptake who would be thyrotoxic.

The curve is actually the ratio of the uptake distribution for thyrotoxic patients to the uptake distribution for the total population sample. It can be shown (see Appendix B) that if both the distribution of the toxic and of the non-toxic uptakes are normal, the resulting curve can be expressed analytically by the equation:

$$T = \frac{1}{1 + k_1 e^{k_2 U^2 + k_3 U + k_4}} \quad [1]$$

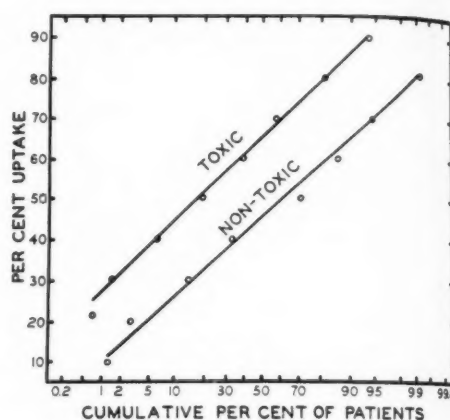


Fig. 2. Distribution of 24-hour thyroid uptakes. Linearity of cumulative plots on probability scale indicates that the distributions are normal.

where T is the fraction of cases that are toxic for a given uptake value, U . The parameters, k_1 , k_2 , k_3 , k_4 , are determined by the standard deviation, mean value, and relative sizes of the two distributions, as shown in Appendix B.

To investigate whether the distributions are normal, the uptake frequency data for toxic and non-toxic patients were plotted in cumulative form on probability paper. As shown in Figure 2, the two distributions can be represented by straight lines, indicating that both are essentially Gaussian (normal). Therefore, an "S"-shaped curve of the type described by Equation [1] should provide a reasonable fit for the data. The " k " values were calculated from the parameter equations given in Appendix B, and the data in Table II, and the curve shown superimposed upon the bars in Figure 1 was derived. Analytically, the curve is represented by the following equation:

$$T = \frac{1}{1 + 1.96e^{-0.000552U^2 - 0.0310U + 3.38}} \quad [2]$$

where T is the fraction of cases that are toxic for a given uptake value, U .

2. *PBI and TPI Values:* In contrast to the thyroidal uptakes, the cumulative plots of the plasma I^{131} values approximated straight lines, not on probability paper, but on logarithmic probability

TABLE II: MEANS AND STANDARD DEVIATIONS

	Non-Toxic (226 Cases)		Toxic (132 Cases)	
	Mean	S.D.*	Mean	S.D.*
Uptake	44.59	14.6	66.99	16.7
Log PBI ¹³¹	-0.9352	0.352	-0.3188	0.404
(Antilog)	(0.116)		(0.480)	
Index	0.184	0.229	0.685	0.262

* Standard deviation of single values (3).

paper, indicating that the logarithms of the plasma I¹³¹ values were more nearly normally distributed than were the raw values. Therefore, the distribution of plasma I¹³¹ data shown in Figure 3 is plotted on a logarithmic scale. The superimposed curve, derived by calculating the parameters in Equation [1], is expressed analytically as follows:

$$T = \frac{1}{1 + 1.96e^{-0.984(\log P)^2 - 5.60(\log P) - 3.22}} \quad [3]$$

where T is the fraction of cases that are toxic for a given PBI¹³¹ value, P .

3. *Combination of Uptake and PBI¹³¹ Values:* For any case included in this study, Equation [2] represents the probability of thyrotoxicosis according to the uptake values, and Equation [3] provides a similar interpretation according to the PBI¹³¹ value. A multiple correlation relating both tests to the observed frequency of toxic cases might provide a more reliable correlation with thyrotoxicosis than either test considered alone. The most straightforward way to find the probability curve would be to make a 3-dimensional plot of the observed frequency of toxic cases as a function of both the uptake and PBI¹³¹ values, and then fit by least squares a suitable 3-dimensional non-linear curve. However, the number of available patient studies for most uptake-PBI intervals was insufficient to justify this method of approach. An alternate method was therefore used which permitted larger grouping of the patients.

First, a correlation was derived between both tests and diagnosis. All non-toxic patients were assigned the "diagnostic index number" 0, and all toxic patients

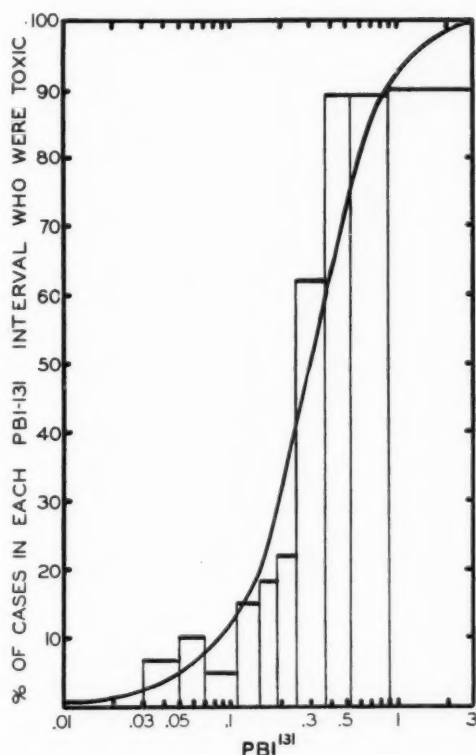


Fig. 3. Incidence of thyrotoxicosis versus 48-hour PBI¹³¹ (or TPI¹³¹; see text). Each vertical bar represents about 35 cases. In addition, there were 6 non-toxic cases with the values less than 0.03 and 4 toxic cases with values greater than 2.9. The curve is plotted from Equation [3].

the diagnostic index number 1.0. A linear multiple correlation equation (3) was then computed with the following result:

$$\text{Diagnostic index} = 0.196 + 0.467(\log \text{PBI}) + 0.00953(\text{uptake}) \quad [4]$$

The coefficient of multiple correlation (3) was 0.71, which was considered reasonably good for a linear fit. A correlation equation was also computed using the PBI¹³¹ values instead of their logarithms. The result had a smaller coefficient of multiple correlation (0.67), giving further support to the decision to use the logarithms of the PBI¹³¹ data in this analysis.

The next step in the analysis of the combined tests was to plot the frequency of thyrotoxic cases as a function of diagnostic index number, computed for each patient

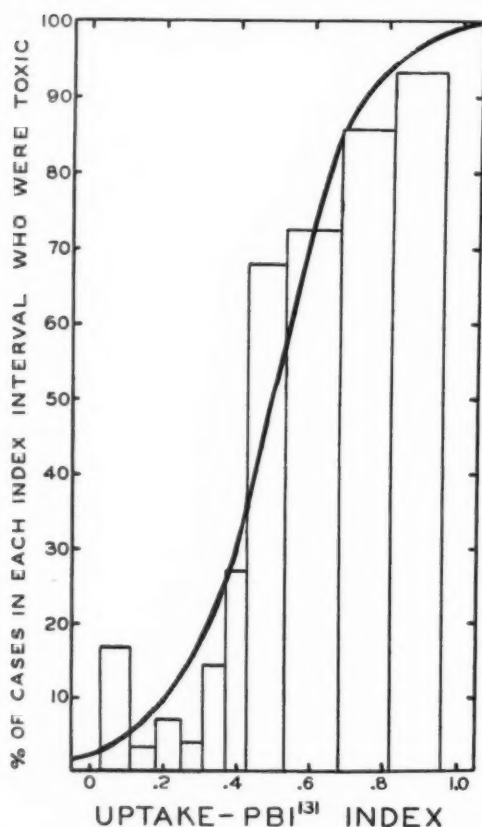


Fig. 4. Incidence of thyrotoxicosis versus diagnostic index number obtained from text Equation [4]. Each vertical bar represents 26 to 30 cases. In addition, there were 53 non-toxic cases with values less than 0.03 and 20 toxic cases with values greater than 0.96. The curve is plotted from Equation [5].

by Equation [4]. The vertical bars in Figure 4 represent the 285 cases having index numbers in the toxic-non-toxic overlap range (0.03 to 0.96), divided into ten approximately equal groups. It was found that plots on probability paper of the cumulative number of toxic and non-toxic cases against diagnostic index number resulted in reasonably straight lines, indicating that an "S"-shaped curve of the type described by Equation [1] would provide a suitable fit to the observed frequency of toxic cases as a function of the calculated index numbers. Therefore, the following curve, also plotted in Figure 4, was computed on the basis of all 358 cases:

$$T = \frac{1}{1 + 1.96e^{-2.25 I^2 - 6.47 I + 3.095}} \quad [5]$$

where T is the fraction of cases that are toxic for a given index value, I , as computed from the PBI^{131} and uptake values with Equation [4]. The coefficients were derived from the parameter equations given in Appendix B. T in Equation [5] can be interpreted as the expected frequency of toxic cases for a population similar to that included in this study. Thus it is possible to predict the "probability" of thyrotoxicosis directly as a function of both the uptake and PBI^{131} values by combining Equations [4] and [5]. A family of curves thus obtained is shown in Figure 5.

4. *Effect of Incidence Factors on the Derived Probability Distribution:* It is obvious that any group of patients referred or selected for thyroid function studies consists of a mixture of two populations (toxic and non-toxic) whose ratio may vary from one institution to another, and from time to time within the same institution. In the material presented here, consisting of a highly selected group of "problem" cases, the ratio of non-toxic to toxic patients was 1.7 to 1. The predicted probability of thyrotoxicosis as a function of uptake and PBI^{131} , as shown in Figure 5, was defined in terms of, and derived from, observed frequency of toxic patients in the population used for this study. In an institution with a markedly different ratio of patients, a quite different diagnostic index distribution would occur even if all other factors were the same, and one would derive a different family of "toxic probability" curves. However, the toxic probability distribution for any given incidence of thyrotoxicosis can be calculated if it is assumed that the distribution of uptake and PBI^{131} values within the toxic and non-toxic groups remains the same and that only the relative size of the two groups changes. To illustrate the "incidence effect" on the probability curves, Equations [4] and [5] were recalculated for non-toxic/toxic ratios

of 1:1 and 5:1. The resulting toxic probability curves are shown in Figure 6.

5. *Thyroid Enlargement, Nodules, and Cardiac Status:* The distribution of PBI^{131} values for euthyroid patients with thyroid enlargement was compared to that of euthyroid patients without thyroid enlargement, and no differences were apparent upon gross inspection. The hyperthyroid group was inspected in the same way, and again no correlation with gland size was apparent. Similarly, the euthyroid and hyperthyroid PBI^{131} distributions were separated according to presence or absence of thyroid nodules, cardiac decompensation, or angina pectoris, and none of these factors appeared to influence the distributions significantly.

When the uptake values were inspected in the same way, two of the subgroup contrasts appeared to be possibly significant. These were tested by computation of the means and standard deviations. The mean of the uptakes of the 60 non-toxic patients with cardiac decompensation was 48.7 ± 1.6 per cent⁴, and of the 166 non-toxic patients without cardiac decompensation was 42.9 ± 1.2 per cent⁴; the difference has high statistical significance ($p < 0.01$). The biological significance of higher uptakes in the cardiac patients is obscure. The finding is in accord with other reports (1, 4) but differs from the observations of Keating *et al.* (5). The only apparent conclusion is that the criteria used to define the cardiac group in our series led to selection of a group of patients with higher uptakes, which may or may not be related to the altered dynamics of their circulation. The other statistically significant subgroup contrast was in the toxic patients, where the mean of the uptakes of the 26 toxic patients with nodular thyroids was 58 ± 2.9 per cent⁴, and of the 106 toxic patients without nodular thyroids was 69 ± 1.5 per cent⁴; this difference has a probability of < 0.001 and is consistent with findings of others (6-8).

6. *Effect of Previous Surgery or I^{131} Treatment:* It is generally recognized that

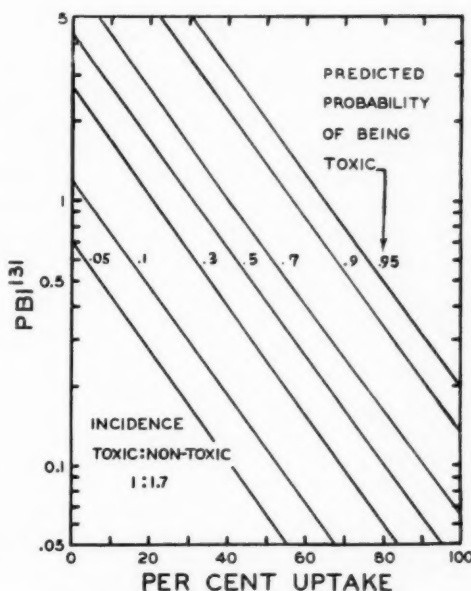


Fig. 5. "Probability" of thyrotoxicosis versus 24-hour thyroidal uptake and 48-hour PBI^{131} .

PBI^{131} values may be elevated in some patients who were previously hyperthyroid and have been rendered euthyroid by surgery or I^{131} treatment, probably because the hormone iodine pool of the thyroid gland is reduced (9, 10). Thirty-one euthyroid and 34 hyperthyroid patients had a history of thyroid surgery or I^{131} treatment. It was expected that inclusion of these patients in the analysis would distort the results, but the contrary was found to be true; separate computation for the 293 patients without such a history yielded a very similar correlation equation:

$$\text{Diagnostic index} = 0.189 + 0.471 (\log PBI) + 0.00954 (\text{uptake}) \quad [6]$$

All 358 cases, therefore, were used in the data analysis, regardless of history of thyroid surgery or I^{131} treatment.

As a corollary to the observations on patients with previous thyroid surgery or I^{131} treatment, it was thought that some information about the relevance of the size of the thyroid hormone iodine pool might be gained by comparing the PBI^{131} values of the toxic patients with enlarged

⁴ Standard error of the mean (3).

thyroids to those of the toxic patients without palpable thyroid enlargement; presumably the latter might have smaller hormone iodine pools and therefore would tend to have higher PBI^{131} values. The mean of the PBI^{131} values for the 92 toxic patients with enlarged thyroids, including all toxic patients with nodular thyroids, was 0.83 ± 0.09 per cent⁴, and for the 40 toxic patients without thyroid enlargement was 0.57 ± 0.09 per cent⁴. The difference is of borderline significance ($p \cong 0.06$) and is in the opposite direction from the hypothesis, *i.e.*, the toxic patients with smaller thyroids have lower PBI^{131} values. The means of the logarithms of the PBI^{131} values for these groups were also compared, and gave a slightly less significant difference ($0.2 > p > 0.1$).

7. *Dependence of Final Diagnosis upon PBI^{131} Factor:* There were 70 cases in which it was thought possible that the PBI^{131} value might have been the deciding factor in determining the final diagnosis, and consideration was given to excluding these cases from the analysis in order to be more certain that the PBI^{131} test was being judged objectively. To conclude that the PBI^{131} determined the diagnosis in nearly 20 per cent of the cases would not be justified, however, since in many cases the same final diagnosis would probably have been made even had no PBI^{131} study been done. As might be expected for this group, the correlation with diagnosis was high for the PBI^{131} values and low for the uptake values, since patients for whom the diagnosis was clearly consistent with the uptake would not be included. A recalculation of the multiple correlation Equation [4] with these 70 cases excluded is as follows:

$$\text{Diagnostic index} = -0.107 + 0.295 (\log PBI) + 0.0132 (\text{uptake}) \quad [7]$$

Compared with Equation [4], Equation [7] gives the uptake greater relative weight since the 70 cases in which the diagnosis was much more consistent with the PBI^{131} than with the uptake have been eliminated. For the final analysis, however, Equation

[4] computed for all cases was used because Equation [7] excludes just those cases in which the PBI^{131} was most useful, and it was believed that in most of these instances the PBI^{131} was actually confirmatory rather than decisive evidence.

DISCUSSION

The purpose of calculating the "toxic probability" curves is to make possible quantitative interpretation of individual test results. For example, if now we have a patient with an uptake of 50 per cent and a PBI^{131} of 0.25, by consulting Figure 5, we would find, on the basis of past experience, that 30 per cent of all such patients may be expected finally to be diagnosed as thyrotoxic.

There are, however, several sources of uncertainty in these calculations:

1. *Sample Selection:* The criteria for selecting the patients for plasma I^{131} determination were clinical and not rigidly defined. There is no way of knowing the extent to which the group upon which this study is based is representative either of the patients who will have plasma I^{131} determinations in this laboratory in the future or of the patients who are tested in other laboratories. The method of correction for incidence of thyrotoxicosis described under the heading Results does not provide for the possibility of a different distribution of uptake and PBI^{131} values within other toxic or non-toxic groups.

2. *"All-or-None" Diagnosis:* Since we could not find any satisfactory way to grade the level of thyroid function in individual patients, the final diagnosis in each case had to be coded as either "toxic" or "non-toxic." In addition to being clinically artificial, this procedure limits the precision of the analysis. It makes it necessary to pool patients over fairly large intervals of uptake and PBI^{131} in order to obtain a reasonable estimate of the frequency of toxicosis for each interval.

3. *The Mixture of PBI^{131} and TPI^{131} Data:* As indicated under the heading

Methods and Case Material, the PBI^{131} was not measured in those cases having a low TPI^{131} . While the PBI^{131} cannot be higher than the TPI^{131} , it can be substantially lower, and we have no way of predicting the $TPI^{131}:PBI^{131}$ ratio. This short cut, therefore, saves considerable labor in the laboratory but might be expected to produce a skew in the distribution of plasma values. The derived curves in Figures 3 and 4 would probably provide a better fit if the PBI^{131} values were known and used in every case.

Limitations of the Statistical Approach

A limitation in applying calculations such as these to the interpretation of individual patient data is the fact that they completely ignore other relevant variables. The elegance of a mathematical correlation of the two tests with diagnosis has an appeal which tends to distract one's attention from the individuality of patients. Such factors as age, diet, renal function, etc., are given no weight in these correlations, yet they may be known in individual cases and should be taken into account in the interpretation of I^{131} tests. Therefore, no matter how reliably one might know the frequency of toxic patients in a given uptake and PBI^{131} interval, this statistical experience should serve as only one facet in the interpretation of test results for an individual patient. It will not be possible to replace the clinician with a computer for the diagnostic interpretation of these tests until sufficient data are available to derive equations which contain all of the variables now considered by the experienced clinical user of I^{131} in diagnostic studies of the thyroid.

Uptake Versus PBI^{131} Reliability

Returning to the original purpose of our study, we can compare the relative usefulness of the two tests in this group of patients by statistical standards. Equation [4] is an estimating equation, by which the uptake and PBI^{131} values are used to estimate the diagnosis. The precision of the result can be expressed in

terms of the standard error of estimate, S.E. (3), which is the root mean square of the difference between the computed indexes and the actual diagnosis (0 or 1). The S.E. for Equation [4] is 0.34. It is a measure of the scatter of index values around their respective diagnoses and implies that about two-thirds of all computed index values will fall within ± 0.34 index units of the correct diagnosis.

Estimating equations similar to [4] but utilizing only uptakes or PBI^{131} data separately are:

$$\text{Diagnostic index} = -0.413 + 0.0148 \text{ uptake} \quad [8]$$

$$\text{Diagnostic index} = 0.818 + 0.634 \log PBI \quad [9]$$

These provide the best fit, by least-squares determination, of the results of the separate tests *versus* the 0 or 1 diagnosis. The S.E. of Equation [8] is 0.39, and of [9] is 0.37, indicating that the log PBI^{131} alone gave a slightly better correlation to diagnosis than did the uptake alone. The combination of both tests, in Equation [4], gave a better correlation than either alone.

Choice of Critical Overlap Values

The toxic probability Equations [2], [3], and [5] can also be used to determine critical overlap values for "toxic" versus "non-toxic." As shown by Newburger *et al.* (2), the minimum number of errors is made when the critical value is taken at the point where the toxic and non-toxic frequency distributions intersect. This is the point where the predicted probability of thyrotoxicosis is 0.5, *i.e.*, where the number of toxic patients having any given test value (uptake, PBI^{131} , or index) is exactly equal to the number of non-toxic patients having that value. In a series which contains more non-toxic than toxic patients, this definition of the critical value will give more false negative than false positive diagnoses of thyrotoxicosis, but the total number of errors will be less than if the critical value were taken at any other point. This definition of critical

TABLE III: ACCURACY OF CRITICAL VALUES

Critical values chosen to give minimum total errors: uptake 61.6%; PBI¹³¹ 0.318%; diagnostic index 0.499

Test	Diagnosis Made by Test					
	Non-toxic		Toxic		Total	
	No.	Correct	No.	Correct	No.	Correct
A. All Cases						
Uptake	256	203 (79%)	102	79 (78%)	358	282 (79%)
PBI ¹³¹	254	214 (84%)	104	92 (88%)	358	306 (85%)
Index	244	211 (86%)	114	99 (87%)	358	310 (87%)
B. Cases in Uptake Range 40-59%						
Uptake	158	120 (76%)	0		158	120 (76%)
PBI ¹³¹	127	114 (90%)	31	25 (81%)	158	139 (88%)
Index	133	115 (86%)	25	20 (80%)	158	135 (85%)
C. Cases in Uptake Range 54-70%						
Uptake	51	27 (53%)	28	17 (61%)	79	44 (56%)
PBI ¹³¹	55	37 (67%)	24	23 (96%)	79	60 (76%)
Index	46	32 (70%)	33	27 (82%)	79	59 (75%)
D. Cases with Previous Thyroid Surgery or I ¹³¹ Treatment						
Uptake	42	29 (69%)	23	21 (91%)	65	50 (77%)
PBI ¹³¹	30	23 (77%)	35	27 (77%)	65	50 (77%)
Index	28	23 (82%)	37	29 (78%)	65	52 (80%)

TABLE IV: ACCURACY OF CRITICAL VALUES

Critical values chosen to give the same proportion of errors in the toxic as in the non-toxic cases: uptake 55.0%; PBI¹³¹ 0.225%; diagnostic index 0.418

Test	Diagnosis Made by Test					
	Non-toxic		Toxic		Total	
	No.	Correct	No.	Correct	No.	Correct
Uptake	210	179 (85%)	148	101 (68%)	358	280 (78%)
PBI ¹³¹	215	192 (89%)	143	109 (76%)	358	301 (84%)
Index	220	200 (91%)	138	112 (81%)	358	312 (87%)

value was used in the analyses summarized in Table III and discussed under 1, below.

A disadvantage of selecting the critical overlap values for minimum number of total misclassifications is that both the overlap value and the per cent error in each group depend upon the relative sizes of the groups. As Billion and Kühne (11), Brinkley *et al.* (12), and Howard *et al.* (13) have shown, in order to evaluate the efficacy of the tests independent of the incidence of thyrotoxicosis and to compare the results with test series of other institutions, the critical overlap value should be chosen so as to produce the same proportion of misclassified cases in each group. This may be done in several ways. Perhaps the simplest method is to find the cross-over point when the numbers of patients in each group are normalized to 100 per cent and plotted as

cumulative frequency curves. When the data for each group are normally distributed and the standard deviations and mean values are known, the critical value may be calculated by the method of Haybittle (14). This was the method used to obtain Table IV, to be discussed in a following section.

When the PBI¹³¹ and uptake data are combined to derive the toxic probability lines shown in Figures 5 and 6, the series of critical values define a "critical line." The critical line which results in the same percentage of misclassified cases in each group is the 0.5 probability line calculated for a toxic to non-toxic incidence ratio of 1:1 shown in Figure 6. In clinical applications, one might prefer to minimize the total number of misclassifications by calculating the 0.5 probability curve for the observed ratio of toxic to non-toxic cases

in one's own institution. For the material presented in this study (ratio 1:1.7), the critical dividing line for minimum error is represented by the 0.5 probability curve shown in Figure 5.

1. Critical Values Selected for Minimum Error:

The critical values obtained in this study for minimum number of misclassified cases are 61.6 per cent for the 24-hour uptake, 0.318 per cent for the 48-hour PBI^{131} , and 0.496 for the diagnostic index number. (The corresponding values obtained by Newburger were 61 per cent for the 24-hour uptake and 0.27 per cent for the 72-hour PBI^{131} .) With these critical values as the sole basis for diagnosis, Section A of Table III shows the number and percentage of the cases that would have agreed with the actual diagnosis. When the cases are separated according to diagnosis in this manner, the PBI^{131} determination appears to be a somewhat more reliable factor than the uptake value, and the diagnostic index which combines both tests appears to have about the same reliability as the PBI^{131} taken alone. The scoring accuracy seems to be about the same for both toxic and non-toxic groups. The accuracy is much less than was found in Newburger's comparable study, but this is not surprising since our material consisted entirely of "problem" cases. The fact that we measured the PBI^{131} at 48 rather than 72 hours should have little effect upon the diagnostic accuracy (9, 15).

We were particularly interested in the value of the PBI^{131} in those patients who had uptakes in the range we had come to regard as equivocal: 40 to 59 per cent (16). The performance of the tests in this group (all below the 62 per cent critical uptake value and hence in the non-toxic uptake region) is shown in Section B of Table III, and indicates that the reliability in this range is only slightly less than in the whole group of patients. The PBI^{131} is more reliable than the uptake, particularly when the PBI^{131} diagnosis is "non-toxic," i.e., when it is in agreement with the uptake. When the PBI^{131} was not in agree-

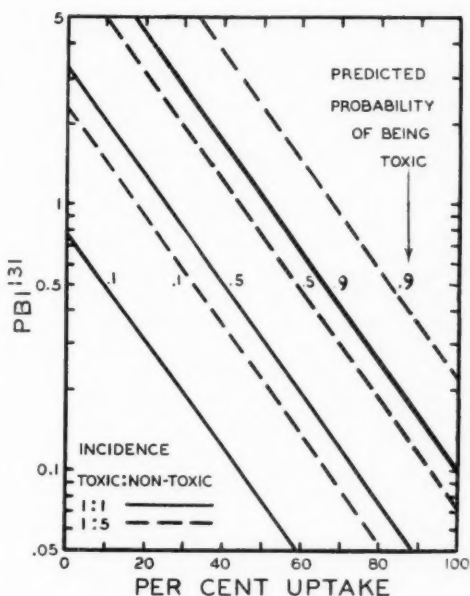


Fig. 6. Examples of the influence of incidence of thyrotoxicosis upon derived "probability" of thyrotoxicosis.

ment with the uptake, it was still correct four times out of five.

The 40 to 59 per cent uptake range corresponds, according to Equation [2], to thyrotoxic probabilities ranging from 0.127 to 0.426. A better choice of an "equivocal" range might be that which includes probabilities from 0.33 to 0.67, which is the 54 to 70 per cent uptake range. Section C of Table III gives the test performances in this range. It is evident that here the uptake reliability is quite poor. The PBI^{131} reliability is substantially better, especially when the result indicates thyrotoxicosis. The diagnostic index has a slightly lower accuracy than the PBI^{131} alone.

The 65 patients who had a history of thyroid surgery or I^{131} treatment were again separated from the total group, for the analysis shown in Section D of Table III. It was demonstrated earlier that omission of these cases from the data would have had very little effect upon the computed index Equation [4], indicating that the distributions of test results for these cases

were similar to those for all cases. It is now seen that the reliability of diagnosis by PBI^{131} or index appears to be somewhat less for these patients considered separately. The decrease in reliability is seen both when the test results are "toxic" and when they are "non-toxic." The hypothesis of a decreased hormone iodine pool mentioned earlier would explain only the false positives. The uptake appears to be considerably more reliable when it is "toxic" in these cases than in the whole group, which is in contrast to the observations of others (9, 12), who found spuriously elevated uptakes in some euthyroid patients who had been previously hyperthyroid. These findings suggest that spurious elevation of the PBI^{131} or uptake after thyroidectomy or I^{131} treatment may occur on occasion but not as a rule.

2. *Critical Values Selected for Equal Percentage Error:* If the critical values are selected to yield the same proportion of errors in the toxic as in the non-toxic group, by the method of Haybittle (14), they are 55.0 per cent for the uptake, 0.225 per cent for the PBI^{131} , and 0.418 for the diagnostic index number. Table IV shows the accuracy of diagnoses based upon these values. It is seen that the overall accuracy is much the same as in Section A of Table III, although in theory more misclassifications would be expected with the method used in Table IV. The distribution of the errors is quite different, however: Table IV shows a substantially higher rate of false positive test results. If the tests were taken as sole criteria, this would result in treatment of a greater number of euthyroid patients for misdiagnosed thyrotoxicosis.

SUMMARY AND CONCLUSIONS

1. In a series of 358 "problem" cases (in which the diagnosis or exclusion of thyrotoxicosis was of greater than average difficulty), the 48-hour plasma I^{131} determination showed a higher correlation with final diagnosis than did the 24-hour thyroidal uptake.

2. A mathematical model was derived

which makes it possible to estimate the probability of thyrotoxicosis for any patient if either the thyroidal uptake or the plasma I^{131} is known. This approach can be applied to any population for which estimates are available of the incidence of the disease and of the means and standard deviations of the test results in toxic and non-toxic patients. The equations which apply to the present series are presented.

To combine the uptake and plasma I^{131} information, a multiple correlation was computed with the aid of a Univac computer. This correlation combines the uptake and plasma I^{131} values for any patient in a single "diagnostic index number." The distribution of these index numbers for the present series was used to calculate an equation (as in the previous paragraph) giving the probability of thyrotoxicosis if both plasma I^{131} and uptake are known.

3. The thyrotoxic probability values derived in this paper may be useful in interpreting individual patient test results, but cannot take the place of a complete evaluation of all clinical signs, symptoms, and laboratory results.

4. Non-toxic cardiac patients had slightly higher thyroidal uptakes than non-cardiacs, and toxic nodular thyroids had lower uptakes than toxic diffuse thyroids. No other correlations were found between the uptake or PBI^{131} and the cardiac status, thyroid size, or thyroid consistency.

5. In patients who had previous thyroid surgery or I^{131} treatment, the percentage of false positives was similar to the percentage of false negatives. Thus post-operative elevation of PBI^{131} or uptake values was not significant for most of these patients.

6. Two methods for selecting a critical value to separate toxic from non-toxic patients are evaluated and their significance is discussed.

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APPENDIX A

PBI¹³¹ Separation Technics

A study was done to intercompare the PBI¹³¹ values obtained by precipitating the plasma proteins with trichloroacetic acid and by removing the inorganic iodide with ion-exchange resins. There was no significant difference in the mean value of 95 determinations obtained by both methods on euthyroid patients. Another intercomparison test was done on the relative extraction efficiencies of the two methods by adding measured amounts of iodide ¹³¹I, ¹³¹I-labeled thyroxine (T-4), and ¹³¹I-labeled triiodothyronine (T-3) to plasma samples. The "resin slurry technic" was found to be 90 to 95 per cent efficient in removing iodide ¹³¹I from plasma, but approximately 10 per cent of the T-3 and T-4 was also trapped by the resin. Precipitation by trichloroacetic acid appeared to be 95 to 100 per cent efficient for removing the labeled T-3 and T-4, but approximately 3 or 4 per cent of the iodide ¹³¹I remained trapped in the precipitate after three washings. Hence, "the resin slurry technic" would be expected to result in slightly lower PBI¹³¹ values than those obtained by the TCA precipitation method for plasma samples containing relatively small percentages of iodide ¹³¹I. Similar efficiency studies were carried out with resin columns, and the results indicated that as much as 20 to 30 per cent of labeled T-3 and T-4 added to serum may be trapped in the column. For that reason, the "resin slurry technic" was retained as the preferred method for this study.

APPENDIX B

Derivation of Equation (1) Used to Fit Data Plotted in Figures 1, 3, 4

Consider two normally distributed groups of values, X and X' , with frequencies Y and Y' , consisting of N and N' number of observations (patients), with standard deviations, s and s' , and with mean values at $x = m$ and at $x = m'$:

$$Y = \frac{N}{s(2\pi)^{1/2}} \exp \left[\frac{-(x-m)^2}{2s^2} \right] \text{ and } Y' = \frac{N'}{s'(2\pi)^{1/2}} \exp \left[\frac{-(x-m')^2}{2s'^2} \right] \quad (1)$$

Let:

$$\beta = -1/2s^2, \quad \text{and} \quad \beta' = -1/2s'^2 \quad (2)$$

Then:

$$\frac{Y'}{Y' + Y} = \frac{1}{1 + Y/Y'} = \frac{1}{1 + k_1 e^{\beta(x-m)^2 - \beta'(x-m')^2}} \quad (3)$$

where:

$$k_1 = Ns'/N's \quad (4)$$

By expanding the terms in the exponent, collecting the coefficients of x and x^2 , we obtain:

$$\frac{Y'}{Y' + Y} = \frac{1}{1 + k_1 e^{k_2 x^2 + k_3 x + k_4}} \quad (5)$$

where:

$$k_2 = \frac{s^2 - s'^2}{2s^2 s'^2} \quad (6)$$

$$k_3 = \frac{s'^2 m - s^2 m'}{s^2 s'^2} \quad (7)$$

$$k_4 = \frac{s^2 m'^2 - s'^2 m^2}{2s^2 s'^2} \quad (8)$$

Equation (5) is the same as Equation [1] in the text. Equations (4), (6), (7), and (8) were used for calculating the k parameters in Equations [2], [3], and [5] in the text and for plotting the curves in Figures 1, 3, and 4.

REFERENCES

1. GORSON, R. O., RAVENTOS, A., ROSE, E., AND CHAMBERLAIN, R. H.: Comparison of the Uptake of Tracer and Treatment Dose of Iodine ¹³¹I by the Thyroid at 24 and 48 Hours. [In] Trans. Am. Goiter A. 1956, Springfield, Ill., Charles C Thomas.
2. NEWBURGER, R. A., SILVER, S., YOHALEM, S. B., AND FEITELBERG, S.: Uptake and Blood Level of Radioactive Iodine in Hyperthyroidism. New England J. Med. **253**: 127-130, July 28, 1955.
3. CROXTON, F. E.: Elementary Statistics with Applications in Medicine and the Biological Sciences. New York, Dover Publications, Inc., 1959.
4. FREEDBERG, A. S., CHAMOVITZ, D. L., AND KURLAND, G. S.: Thyroid Function in Normal and Pathological States as Revealed by Radioactive Iodine Studies. I: Thyroid ¹³¹I Uptake and Turnover in Euthyroid, Hyperthyroid and Hypothyroid Subjects. Metabolism **1**: 26-35, January 1952.
5. KEATING, F. R., JR., HAINES, S. F., POWER, M. H., AND WILLIAMS, M. M. D.: The Radioiodine-Accumulating Function of the Human Thyroid Gland as a Diagnostic Test in Clinical Medicine. J. Clin. Endocrinol. **10**: 1425-1464, November 1950.
6. LARSSON, L. G.: Studies on Radioiodine Treatment of Thyrotoxicosis with Special Reference to the Behaviour of the Radioiodine Tracer Tests. Acta radiol. Suppl. 126, 1955.
7. GOODWIN, J. F., MACGREGOR, A. G., MILLER, H., AND WAYNE, E. J.: The Use of Radioactive Iodine

in the Assessment of Thyroid Function. *Quart. J. Med.* **20**: 353-387, October 1951.

8. SEED, L., AND JAFFÉ, B.: Results of Treatment of Toxic Goiter with Radioactive Iodine. *J. Clin. Endocrinol.* **13**: 107-119, January 1953.

9. QUMBY, E. H., FEITELBERG, S., AND SILVER, S.: *Radioactive Isotopes in Clinical Practice*. Philadelphia, Lea & Febiger, 1958.

10. BERSON, S. A., AND YALOW, R. S.: Quantitative Aspects of Iodine Metabolism. The Exchangeable Organic Iodine Pool, and the Rates of Thyroidal Secretion, Peripheral Degradation and Fecal Excretion of Endogenously Synthesized Organically Bound Iodine. *J. Clin. Invest.* **33**: 1533-1552, November 1954.

11. BILLION, H., AND KÜHNE, P.: Der Wert verschiedener Radiojodtestverfahren für die Differentialdiagnostik von Schilddrüsenfunktionsstörungen. *Ztschr. f. klin. Med.* **152**: 411-433, 1954.

12. BRINKLEY, D., HAYBITTLE, J. L., AND PLESTED, K. J.: Some Results of Radio-Iodine Diagnostic Tests for Thyroid Function. *Acta radiol.* **48**: 33-51, July 1957.

13. HOWARD, N., FIELD, E. O., AND DYCHÉ, G. M.: A Comparison of the 15-Minute Continuous Thyroid Uptake Test with Other Radioiodine Tests. *Brit. J. Radiol.* **33**: 316-320, May 1960.

14. HAYBITTLE, J. L.: Letter to the Editor. *Brit. J. Radiol.* **33**: 529, August 1960.

15. MCCONAHEY, W. M., KEATING, F. R., JR., AND POWER, M. H.: The Behavior of Radioiodine in the Blood. *J. Clin. Invest.* **28**: 191-198, March 1949.

16. RAVENTOS, A., HALE, J., AND CHAMBERLAIN, R. H.: Two-Hour Uptake of Iodine 131 by the Thyroid. *Radiology* **75**: 446-449, September 1960.

SUMMARY IN INTERLINGUA

Determination de I^{131} in le Plasma e del Acceptation de I^{131} per le Thyroide in Le Diagnose de Casos "Problematic" de Hyperthyroidismo

In un serie de 358 cases "problematic," in le quales le diagnose del presentia o absentia de thyrotoxicosis esseva plus que mediemente difficile, le determination del I^{131} del plasma post 48 horas monstrava un plus alte correlation con le ultime diagnose que le determination del I^{131} acceptate per le thyroide in 24 horas.

Esseva derivate un modello mathematic que permette estimar le probabilitate de thyrotoxicosis in omne patiente individual si on cognosce (1) le acceptation thyroide o (2) le concentration plasmatic de I^{131} . Le methodo pote esser applicate a non importa qual population pro le qual estimatos es disponibile de (1) le incidentia del morbo e (2) le valores medie e le deviationes standard del resultados de tests in patientes con e sin thyrotoxicosis. Es presentate le equationes que es applicabile al presente serie.

Pro combinar le informationes in re le acceptation thyroide e le concentration plasmatic de I^{131} , un correlation multiple esseva computate con le adjuta de un calculator electronic Univac. Iste correlation combina le valores del acceptation thyroide e del concentration plasmatic de I^{131} pro omne patiente particular in un sol "diagnostic indice numeric." Le distribution del indices numeric pro le casos in le presente serie esseva usate pro derivar un equation que exprime le probabilitate de

thyrotoxicosis si le acceptation thyroide e etiam le concentration plasmatic de I^{131} es cognoscite.

Le valores del probabilitate de thyrotoxicosis derivate in iste communication es utile in interpretar le resultados de tests in patientes individual, sed illos non pote reimplaciar le evaluation complete de omne le signos e symptomas clinic e del resultados de omne le altere studios laboratorial.

Non-toxic patientes cardiac habeva levemente plus alte valores pro le acceptation thyroide de I^{131} que non-toxic patientes non-cardiac, e toxic thyroides nodular habeva plus basse acceptationes que toxic thyroides diffuse. Nulle altere correlationes esseva trovate inter le acceptation de I^{131} o le concentration de I^{131} ligate a proteina e le stato cardiac, le dimensiones del thyroide, o le consistentia thyroide.

In patientes previamente submittite a chirurgia thyroide o a tractamento con I^{131} , le procentage de resultados falsemente positive esseva simile al procentage de resultados falsemente negative. Assi un elevation post-operatori del valores pro I^{131} ligate a proteina o pro le acceptation thyroide de I^{131} non esseva significative in le majoritate de iste patientes.

Duo methodos pro le selection de un valor critic que differentia inter patientes toxic e non-toxic es evaluate.

Percutaneous Transfemoral Renal Arteriography in Hypertension¹

MORDECAI HALPERN, M.D., NATHANIEL FINBY, M.D., and JOHN A. EVANS, M.D.

RENAL ARTERIOGRAPHY finds its most important application in the study of renal hypertension. The modified Seldinger technic (1) of percutaneous transfemoral retrograde arteriography provides a precise and accurate demonstration of the anatomy and vascular pathology of the renal arteries and their intrarenal branches. In addition, a nephrographic phase during the study reflects the status of the renal parenchyma.

The radiologic demonstration of the anatomic-pathologic state of the renal vessels is mandatory for the surgical approach to remediable lesions. A recent study (2) in which aortography was used extensively in hypertensive patients demonstrated lesions of occlusive renal arterial disease in about 25 per cent of the total. The occlusive lesion was considered to be the primary cause of the hypertension in the majority. Occlusive renal arterial disease is listed as the most common cause of hypertension which is amenable to surgical correction, and at this time, 75 (3) to 82 per cent (4) of patients have been made normotensive following appropriate surgery.

MATERIAL AND METHODS

The clinical material forming the basis for this report comprises the first 41 cases studied following the adoption of the percutaneous transfemoral technic of Seldinger by the Department of Radiology at The New York Hospital-Cornell Medical Center. In 4 cases the catheter was passed through a femoral arteriotomy that was deemed clinically advisable.

Completely adequate pre-examination medication for the percutaneous method

has consisted in the administration of 50 to 100 mg. of soluble phenobarbital intramuscularly. Thirty-seven of 38 patients underwent examination by an attending radiologist with passage of the transfemoral catheter under local procaine anesthesia. In one instance, a tense, nervous seventeen-year-old boy was studied under general anesthesia. Precautionary post-examination steps have consisted of inguinal pressure dressings and bed rest for approximately six hours. There have been no complications except for two minimal subcutaneous hematomas.

Pre-arranged catheter lengths have made fluoroscopy unnecessary. The detailed anatomic study of angioneurography by Edsman (5) has made this pre-arrangement possible. A test film has been utilized to check and correct the position of the tip of the catheter before injection of the contrast medium and the start of the serial filming procedure. In a few instances the guide wire or catheter was inadvertently passed into the deep circumflex iliac artery or the common iliac of the contralateral side. In these cases the catheter was easily readjusted or passage was made through the opposite femoral artery.

The hand-operated Lehman and mechanical Cordis or Gidlund injectors have been used to instill the organic iodide contrast agent. The mechanical pressure injectors are superior, since they allow a more delicate pressure control and a greater flow rate of the opaque medium in terms of cubic centimeters per second. The Cordis Intercalative Angiograph (Cordis Corporation, Miami, Fla.) is probably the most efficient of these, since it is a completely

¹ From the Department of Radiology, The New York Hospital-Cornell Medical Center, New York, N. Y. Aided by a grant from the Whitehall Foundation.

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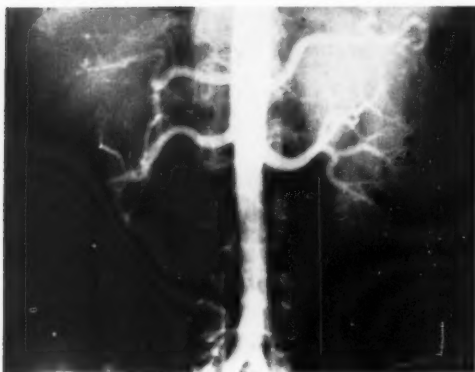


Fig. 1. Normal renal arteriogram.

self-contained hydraulic system which provides excellent pressure control, and may be intercalated with the electrocardiographic recording.

Patients tolerate the procedure without discomfort, although minor fleeting sensations of warmth are usually noted in the abdomen and back at the time of injection. It should be stressed that this is a safe, simple, and precise method for selective radiographic visualization of the pertinent vessels (Fig. 1). There has been no patient morbidity.

The basic indications for arteriography in hypertensive patients have been logically categorized by Poutasse (3, 6). We have utilized the following indications for our studies:

1. Hypertension in a patient under the age of fifty with no other demonstrable cause.
2. Development of malignant hypertension or sudden development of hypertension at any age.
3. Hypertension that first appears or increases following an episode of flank pain or following abdominal trauma.

In addition, accurate visualization of the renal arteries is mandatory when differential renal excretion studies reveal more than 15 per cent decrease in the excretion of sodium and/or a 50 per cent drop in water output (7, 8).

Incidentally, we have found an excellent application of this technic in special problems related to the renal parenchyma and

have established a definite diagnosis of renal carcinoma in 2 patients by demonstration of abnormal vessels within a renal mass. Of additional interest are 2 patients in whom clinicians were reluctant to accept a correct nephrotomographic diagnosis of renal cyst in one and of a normal kidney in another, choosing to recommend exploratory surgery. Following diagnostic confirmation by renal arteriography, the contemplated surgical procedures were abandoned.

CASE MATERIAL

In our limited series of cases we have visualized examples of the most important pathologic entities representing the remediable lesions of the renal arteries associated with hypertension (3, 9, 10, 12). A simple pathologic classification of the major lesions in our patients is as follows:

I. Fibromuscular hyperplasia with associated segmental stenosis, as described in young patients by McCormack (9), Harnaes (11), De Camp (12), and Leadbetter (20), in 5 patients (Figs. 2-5).

II. Arteriosclerotic plaques with or without poststenotic dilatation, in 7 patients (Figs. 6 and 7).

III. Complete occlusion of a renal artery with atrophy of the kidney, in 2 patients (Fig. 8).

IV. Thrombosis or embolism, in 2 patients (Fig. 9).

V. Miscellaneous. One patient had hypertension associated with chronic pyelonephritis. Two additional patients had diminished function and reduced vascularity in an atrophic kidney. In 1 patient a small partially calcified right renal artery aneurysm was revealed.

In the arteriosclerotic group it is most important to recognize that such lesions may be bilateral in a third of the cases (2) and that associated aortic-iliac disease will be present in about 75 per cent, as reported by Morris *et al.* (4). These authors also noted a somewhat insidious development of the hypertension, and the existence of the hypertensive state for some years before surgery.

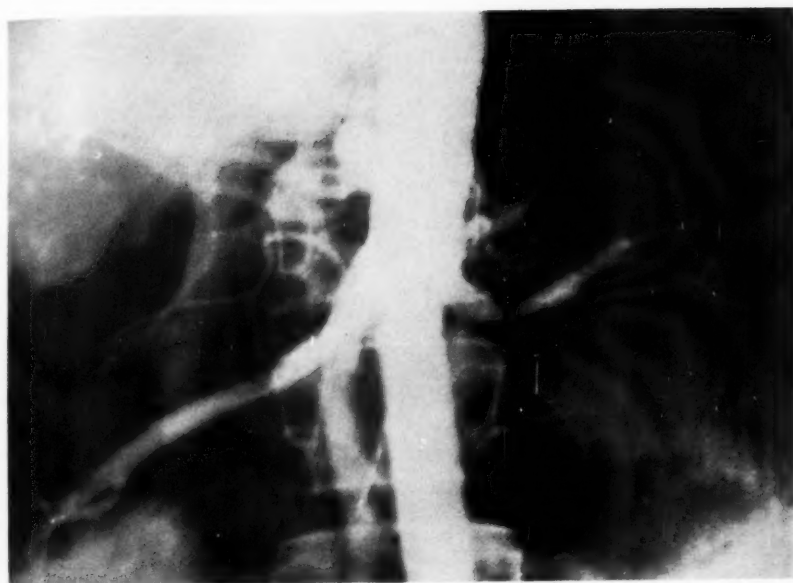


Fig. 2. "Coarctation" of the left renal artery, in a seventeen-year-old male. Blood pressure 170/130. Clinical diagnosis of primary hyperaldosteronism was established. Total adrenalectomy failed to relieve hypertension and left nephrectomy was performed six months later. Blood pressure two weeks postoperatively 138/94 with subsequent return to normotensive state.



Fig. 3. Annular constriction of left renal artery (arrow) with poststenotic dilatation in a thirty-year-old male. Blood pressure 156/120, associated with sudden blindness in the right eye. Right internal carotid endarterectomy followed by left splenorenal shunt. Blood pressure three weeks postoperatively 110/80. Patient has remained normotensive.

Though the surgical treatment is beyond the scope of this report, it is, nonetheless, the ability of our surgical confreres that makes precise radiologic visualization of the renal vessels essential. The 75 to 82 per cent return to a normotensive state previously mentioned is in striking contrast to the results recorded before 1954, when a satisfactory fall in blood pressure did not occur in more than 20 per cent of the cases (3, 4).

reduction in urine volume from the affected kidney. Eight of these patients underwent nephrectomy. In a second group of 8 cases, urine volume was lowered but the sodium concentration was equal to or greater than that on the normal side. Nephrectomy resulted in no change in the hypertensive status of this group. If these patients had stenotic arterial lesions, it would seem that surgical revascularization might have been an effective and

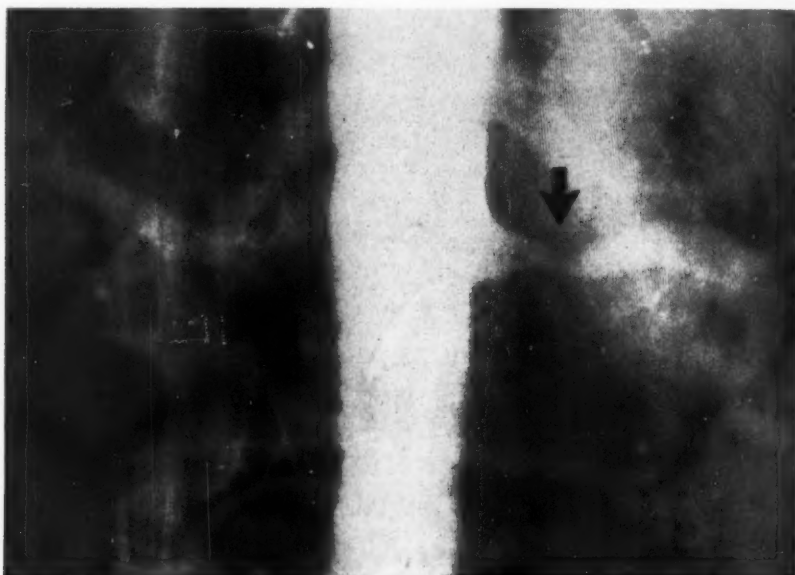


Fig. 4. Annular constriction with poststenotic dilatation in a forty-year-old male. Blood pressure 240/120. Left renal by-pass performed with graft. Return to sustained normotension in one week.

The current basic surgical techniques (4, 8, 12) have been directed toward the goal of revascularization of the kidney, as opposed to nephrectomy, and consist of endarterectomy, resection with graft replacement, and splenorenal arterial anastomosis. Morris (4) reports greater use of a by-pass with graft and, when feasible, direct renal artery patch reconstruction.

A recent review by Connor (7) of the role of differential ureteral catheterization studies in unilateral renal hypertension revealed excellent results in 9 patients who had at least a 15 per cent reduction in sodium concentration and a 50 per cent

preferable method of treatment. Indeed, the constricting arterial lesion tends to protect the kidney, while it is in the contralateral kidney that nephrosclerotic changes develop (13-15). It thus seems quite clear that these patients require careful, exacting radiologic examination of the renal arteries.

DISCUSSION

Percutaneous transfemoral catheter arteriography is a diagnostic procedure which, with reasonable precaution, appears to be without complication. Its simplicity of execution and the excellence of the renal arteriogram make it a highly desirable

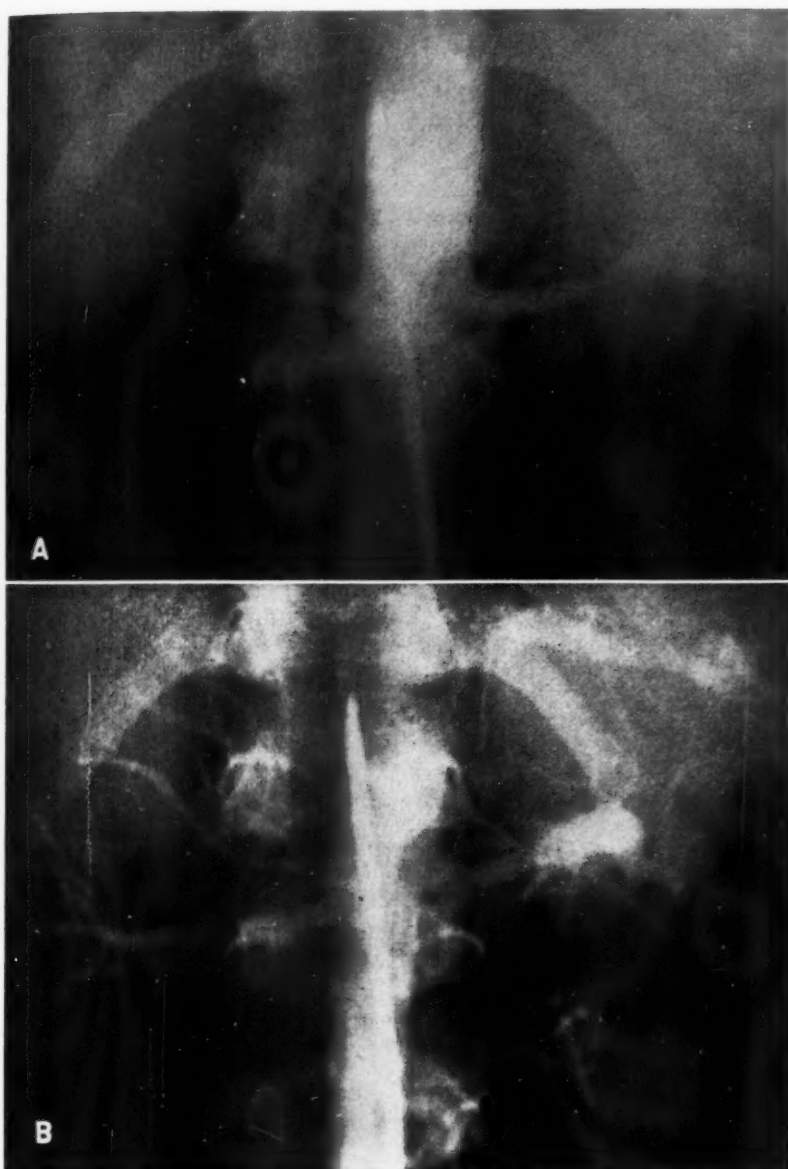


Fig. 5. "Coarctation" of the left renal artery in a thirteen-year-old male. Blood pressure 180/120. Splenorenal shunt performed with return to normotension in one week. Note jet through stenotic area in A and poststenotic dilatation in B.

technic in the investigation of the hypertensive patient suspected of harboring a renal artery lesion. Of great importance is the elimination of the hazards inherent in the comparable diagnostic technic of lumbar aortography. Fatalities, though

rare, have been reported, and serious complications with the translumbar technic (16, 17) have occasionally been recorded in the literature. While the Seldinger method has been used extensively abroad, its advantages do not yet appear to have been

fully appreciated by American radiologists. In a recent publication, Luke (8) states that this method has supplanted the translumbar technic at the Royal Victoria Hospital in Montreal. Dotter has also utilized it to advantage (18).

We have been impressed by the coexistence of cerebrocarotid insufficiency and arteriosclerotic carotid plaques in a significant number of patients, the majority of whom have been in the fourth and fifth

renogram or differential renal function studies in the investigation of renal hypertension. We do regard the latter as an integral part of the diagnostic work-up.

With regard to the radioactive Diodrast renogram, we have had only general experience in various renal diseases, including hypertension, at The New York Hospital-Cornell Medical Center (19). It is our opinion at this time that, while this method may be a useful adjunctive study,



Fig. 6. Bilateral arteriosclerotic plaques (arrows) with marked poststenotic dilatation on the right and severe arteriosclerosis of the abdominal aorta. Blood pressure 200/120. Operation: right renal by-pass with Teflon graft to the right common iliac artery. Blood pressure four weeks postoperatively, 160/90.

decades of life. Indeed, one hypertensive forty-year-old man died of a cerebrovascular accident one day before scheduled arteriography. Two patients, one thirty years old (Fig. 3) and another forty years old, required a carotid endarterectomy prior to surgical treatment of their renal artery lesions. A third patient, also aged forty (Fig. 4), presented with such a characteristic clinical picture of incomplete cerebral vascular thrombosis that immediate carotid exploration was performed.

As of this moment our experience is too limited to enable us to evaluate properly the definitive role of the I^{131} Diodrast

main reliance must still be placed on established procedures, the most important of which is renal arteriography. Of the patients undergoing Diodrast renography, 2 showed a hypovascular kidney and 1 a disturbance of secretory function; in another, there was no evidence of hypovascularity.

In the past few years, large series of patients with occlusive renal vascular lesions showing the excellent results of surgical treatment have been reported in the literature. We have been impressed by the relative sparsity of reports of the occlusive lesion of the young patient de-

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Fig. 7. Bilateral arteriosclerotic plaques (arrows) with severe narrowing of the left renal artery. Blood pressure 236/110. Patient awaiting remediable surgery through by-pass grafts.



Fig. 8. Complete occlusion of left renal artery treated by nephrectomy.

scribed as a fibromuscular subintimal proliferation or fibromuscular hyperplasia of the arterial wall (9, 12, 20). A segmental stenotic lesion of this type was discovered by Harnaes and Seip (11) in an

eleven-year-old boy. Luke's group of patients (8) contains 2 cases, one in a thirty-six-year-old man and a second in a forty-year-old woman. It should be noted that we are being presumptive as to the

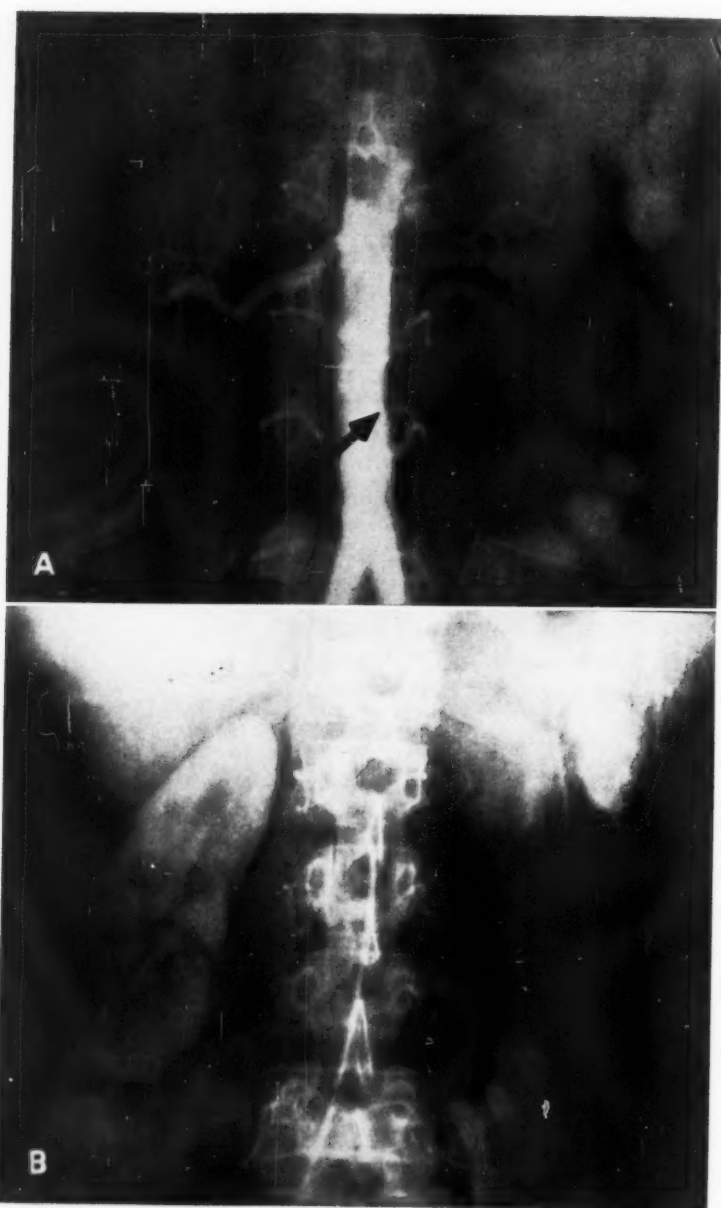


Fig. 9. A. Thrombosis of accessory left renal artery (arrow). B. Note reduced nephrogram density on left and lack of nephrogram in lower half of the kidney.

exact nature of the pathologic process since in most instances of surgery in renal hypertension, pathologic specimens are not made available. However, the roentgenographic picture of the stenotic lesion (Figs.

2-5) in a younger patient seems to be quite characteristic and is, for the most part, not associated with evidence of generalized arteriosclerotic disease.

A recent report of 3 cases treated by

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excision of the diseased segment and an end-to-end arterial anastomosis has provided excellent confirmation of this pathologic entity (21). Certainly, in light of the excellence of surgical results, the radiologist should adopt an aggressive diagnostic approach to these problems and actively participate in the management of the clinical problems.

We would draw special attention to our patient with clinical evidence of hyperaldosteronism who continued to exhibit hypertension after total adrenalectomy (Fig. 2). The experience with this patient indicates the advisability of supplementing the roentgenologic work-up in cases of aldosteronism, and perhaps even pheochromocytoma, with percutaneous transfemoral renal arteriography before surgery.

SUMMARY

1. Percutaneous transfemoral retrograde arteriography has been added to the diagnostic studies done in the Department of Radiology at The New York Hospital-Cornell Medical Center because it provides precise, selective visualization of the renal arteries with a minimum of hazard.

2. A summation of the basic indications for renal arteriography, the vascular pathology involved, and the operative approach has been given.

3. Selection of hypertensive patients for renal arteriography is advised. In our series, 49 per cent of these selected patients showed a variety of lesions, several of which are illustrated. Twenty-four per cent of these hypertensive patients with remediable lesions were below forty years of age.

ADDENDUM: Since this paper was submitted for publication, the total of patients studied has reached 130. Thirty-four per cent of the surgical remediable lesions have been in patients under forty years of age.

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REFERENCES

1. SELDINGER, S. I.: Catheter Replacement of the Needle in Percutaneous Arteriography. A New Technique. *Acta radiol.* **39**: 368-376, May 1953.
2. POUTASSE, E. F.: Surgical Treatment of Renal Hypertension: Results in Patients with Occlusive Lesions of Renal Arteries. *J. Urol.* **82**: 403-411, October 1959.
3. DUSTAN, H. P., PAGE, I. H., AND POUTASSE, E. F.: Renal Hypertension. *New England J. Med.* **261**: 647-653, Sept. 24, 1959.
4. MORRIS, G. C., JR., DE BAKEY, M. E., COOLEY, D. A., AND CRAWFORD, E. S.: Surgical Treatment of Renal Hypertension. *Ann. Surg.* **151**: 854-866, June 1960.
5. EDSMAN, G.: Angionephrography and Suprarenal Angiography. A Roentgenologic Study of the Normal Kidney, Expansive Renal and Suprarenal Lesions and Renal Aneurysms. *Acta radiol. Suppl.* **155**, 1957.
6. POUTASSE, E. F., AND DUSTAN, H. P.: Arteriosclerosis and Renal Hypertension. Indications for Aortography in Hypertensive Patients and Results of Surgical Treatment of Obstructive Lesions of Renal Artery. *J.A.M.A.* **165**: 1521-1525, Nov. 23, 1957.
7. CONNOR, T. B., THOMAS, W. C., JR., HADDOCK, L., AND HOWARD, J. E.: Unilateral Renal Disease as a Cause of Hypertension: Its Detection by Ureteral Catheterization Studies. *Ann. Int. Med.* **52**: 544-559, March 1960.
8. LUKE, J. C.: The Useful Splenic Artery. *Surg., Gynec. & Obst.* **110**: 633-638, May 1960.
9. McCORMACK, L. J., HAZARD, S. B., AND POUTASSE, E. F.: Obstructive Lesions of the Renal Artery Associated with Hypertension. *Am. J. Path.* **34**: 582, May-June 1958.
10. GLAZIER, M., and LOMBARDO, L. J., JR.: Diseases of Renal Artery. *J. Urol.* **81**: 27-34, January 1959.
11. HARNAES, K., AND SEIP, M.: Unilateral Kidney Disease with Hypertension in Children. *Acta paediat.* **49**: 28-38, January 1960.
12. DE CAMP, P. T., AND BIRCHALL, R.: Recognition and Treatment of Renal Arterial Stenosis Associated with Hypertension. *Surgery* **43**: 134-151, January 1958.
13. LA FORET, E. G.: Malignant Hypertension Associated with Unilateral Renal Artery Occlusion. Three Cases. *Ann. Int. Med.* **38**: 667-688, April 1953.
14. BAUER, H., AND FORBES, G. L.: Unilateral Renal Artery Obstruction Associated with Malignant Nephrosclerosis Confined to Opposite Kidney. *Am. Heart J.* **44**: 634-638, October 1952.
15. GOODMAN, H. L.: Malignant Hypertension with Unilateral Renal Artery Occlusion. *New England J. Med.* **246**: 8-12, Jan. 3, 1952.
16. GREGG, D. M., ALLCOCK, J. M., AND BERRIDGE, F. R.: Percutaneous Transfemoral Selective Renal Arteriography (Including Cineradiology). *Brit. J. Radiol.* **30**: 423-435, August 1957.
17. STEINBERG, I., FINBY, N., AND EVANS, J. A.: A Safe and Practical Intravenous Method for Abdominal Aortography, Peripheral Arteriography and Cerebral Angiography. *Am. J. Roentgenol.* **82**: 758-772, November 1959.
18. DOTTER, C. T.: Left Ventricular and Systemic Arterial Catheterization: A Simple Percutaneous Method Using a Spring Guide. *Am. J. Roentgenol.* **83**: 969-984, June 1960.
19. POKER, N., MARSHALL, V. F., BECKER, D. V., AND EVANS, J. A.: The Radioisotope Renogram: A Clinical Evaluation and Some Theoretical Aspects. *Am. J. Roentgenol.* **84**: 866-875, November 1960.
20. LEADBETTER, W. F., AND BURKLAND, C. E.: Hypertension in Unilateral Renal Disease. *J. Urol.* **39**: 611-626, May 1938.
21. WYLIE, E. J., AND WELLINGTON, J. S.: Hypertension Caused by Fibromuscular Hyperplasia of the Renal Arteries. *Am. J. Surg.* **100**: 183-193, August 1960.

SUMMARIO IN INTERLINGUA

Arteriographia Percutaneo-Transfemoral in Hypertension Renal

Arteriographia renal ha su plus importante application in le studio de hypertension renal. Arteriographia retrograde percutaneo-transfemoral provide un precise visualisation selective del arterias renal con un minimo de risco. Le methodo ha essite usate per le autores in casos con le sequente indicationes: Hypertension in subjectos con minus que cinquanta annos de etate in le absentia de altere demonstrabile causas; le disveloppamento de hypertension maligne o le subite disveloppamento de hypertension a non importa qual etate; hypertension que se disveloppa o augmenta post un episodio de dolor del fianco o trauma abdominal. Accurata del visualisation es indispensable etiam quando studios differential del excretion del renes revela un reduction per plus que 15 pro cento in le excretion de natrium e/o un reduction per 50 pro cento in le rendimento de aqua.

Le selection del patientes pro arterio-

graphia renal es a recommendar. In le seligite serie del autores, amontante a un total de 41 casos (incluse 24 pro cento con etates de minus que quaranta annos), 49 pro cento monstrava un varietate de lesiones.

Le importante entitates pathologic representante remediabile lesiones del arterias renal esseva (1) hyperplasia fibromuscular con associate stenosis segmental in 5 patientes, (2) placas arteriosclerotic con o sin dilatation poststenotic in 7 patientes, (3) occlusion complete de un arteria renal con atrophie del ren in 2 patientes, (4) thrombose o embolismo in 2 patientes, e (5) un numero de conditiones miscellaneas.

Le facto que le retorno a un stato normotensive es possibile in un alte procentage de patientes post le appropriate intervention chirurgic rende le precise visualisation radiologic del arterias renal un desiderato urgentissime.



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Radiation Therapy in Breast Cancer: Optimal Combination of Technical Factors; Analysis of Five-Year Results¹

NORA G. DE MOOR, M.B.B.Ch., D.M.R., DAVID DURBACH, M.A., M.R.C.S., L.R.C.P., D.M.R.T., JOSEPH LEVIN M.B.B.Ch., D.M.R.T., and LIONEL COHEN, Ph.D., M.B.B.Ch., D.M.R.T.

ALTHOUGH BOTH mastectomy and radiation have been used in the treatment of breast cancer for over half a century, there is still no unanimity among surgeons or radiotherapists as to the value of such treatment in general, much less as to the relative merits of the two modalities and the various technical differences in the application. According to some authorities (49, 58), it is doubtful whether the average survival of patients with breast cancer can be improved by any form of therapy currently available, be it radical surgery or radiation therapy, although the palliative value of treatment for the locally advanced or metastatic stages of the disease is generally accepted. Whether a combined procedure can achieve more than either modality alone or, more specifically, the extent to which radiation can improve upon the overall salvage rate with surgery alone, remains obscure. Before any form of therapy can be assessed, therefore, it is necessary to define its objectives and limitations.

There is some evidence (54) that the survival time is significantly prolonged in treated patients as compared with an untreated series. The average duration of life in untreated cases is approximately forty months from the onset of symptoms (10, 24, 30, 54, 65, 68) and the five-year survival rate is in the region of 16 to 20 per cent (1, 34). In treated series the overall five-year survival averages around 35 per cent, ranging from 55 per cent for early cases to 15 per cent for later stages (6, 57, 62, 67). It is an interesting fact that, in spite of the widely different surgical procedures employed, including radical and supradical mastectomies, local mastectomy with or without axillary node dis-

section, and even simple excision of the tumor alone, and the varied radiotherapy techniques and dosages, the five-year survival rates, when corrected for the relative proportions of early and late cases, are essentially the same at different centers (6, 57). The survival rate has also remained fairly constant, irrespective of technical advances over the years. It seems unlikely at present that any further developments in technique, either in surgery or in radiation therapy, could improve upon these figures substantially. The outcome is determined in most instances by the degree of dissemination of the tumor and is independent of the exact surgical or radiotherapeutic measures employed (57, 58).

A significant proportion of surviving patients will have locally persistent or recurrent cancer in the chest wall or regional lymph nodes. The question then arises as to whether improved techniques can reduce the local recurrence rate, without adversely affecting the overall five-year survival. If any particular radiotherapeutic procedure can achieve this, then radiation is justifiably applied as a radical treatment or adjunct in the management of breast cancer, in addition to its obvious role in palliation of advanced disease.

Since over 60 per cent of all patients presenting for treatment inevitably die of disseminated metastatic cancer within five years, only that fraction of the surviving 40 per cent in whom local recurrence would develop could benefit from such prophylactic radiotherapy. Local recurrence rates following surgery, either alone or combined with irradiation, range from a minimum of about 10 per cent in some treated series (7, 34)—the average for early cases being

¹ From the Radiation Therapy Department, General Hospital, Johannesburg, Union of South Africa. Accepted for publication in October 1960.

18 per cent (13, 38, 48, 50)—to over 40 per cent if more advanced and inoperable cases are included (31, 46, 29). On the basis of average figures, therefore, it seems that, out of every 100 patients presenting for treatment, there will be about 40 five-year survivors, 7 to 16 of whom will have locally persistent or recurrent tumour. Only in this relatively small group of cases is eradication of the local disease by irradiation of any curative value, and such a marginal gain must necessarily be the prime objective of radical radiation therapy.

It is possible, on the other hand, that radical methods for elimination of local recurrences might diminish the overall five-year survival rate, because of local complications or possibly through a lowered systemic resistance to the tumour. In view of some recent disturbing evidence for such an effect, particularly in the younger age group and early stages (50, 62), it has been suggested (50) that in clinical and pathological Stage I breast cancer in younger women subject to radical mastectomy, it might be advisable to withhold postoperative irradiation until obvious recurrence is manifest. Against this must be weighed the low recurrence rate we have encountered after our routine postoperative prophylactic radical radiotherapy to be described below, and the usually poor prognosis of patients treated after local recurrence has become evident (48).

SURGICAL PROCEDURES

Although it is not the object of this paper to analyse the various surgical procedures which have been advocated in the treatment of mammary cancer, the nature of the operation necessarily influences the selection and design of the radiotherapeutic modality. This must vary according to the surgical policy in relation to the stage of the disease, criteria of operability, and the extent of the operative procedure adopted. Since there is no conclusive evidence proving the superiority of any one surgical approach (6), it has been necessary to maintain a degree of flexibility in the radiotherapeutic regime.

Treatment may have to be adjusted according to prevailing surgical fashion, as well as in response to newer knowledge of methods for improving immediate results and avoiding undesirable sequelae.

In general, the early or operable cases have had a classical radical or a total local mastectomy, followed by referral for postoperative irradiation to the chest wall and regional nodes. Some surgeons prefer more radical procedures, leaving a thin chest wall devoid of subcutaneous tissue, often carrying precarious skin grafts unable to tolerate full effective doses of radiation; in these cases radiotherapy must be directed to the regional nodes but not to the chest wall. Some inoperable cases, without distant metastases, are referred for irradiation of the whole affected area as the sole method of treatment; in others, ostensibly inoperable, a limited mastectomy may have been performed, designed to facilitate subsequent radical irradiation of the chest wall. Advanced and incurable cases, with extension or metastasis beyond the primarily affected region, are referred for palliative irradiation without any attempt at surgical removal.

IRRADIATION OF THE REGIONAL NODES

It is generally accepted that the regional nodes constituting the first phalanx of lymphatic spread in breast cancer—namely, the axillary, supraclavicular, and internal mammary chains—are amenable to irradiation with high-voltage roentgen rays. These are usually directed through three standard portals: sternal, anterior supraclavicular and axillary, and posterior axillary fields. One such arrangement, which we have adopted, is shown in Figure 1, in which portals 1, 2, and 3 represent the three fields described. Suitable technical factors are 250 kv constant potential, Thoraeus filter (0.4 mm. Sn + 0.25 mm. Cu + 1.0 mm. Al), giving a half-value layer of 3 mm. Cu, and a focus-skin distance of 50 cm.

Since the internal mammary nodes are about 2 cm. deep and not more than 4 cm. from the midline (27), a single sternal field

measuring 15×7.5 cm. will subtend both internal mammary chains, the nodes falling well within the 80 per cent isodose line. The anterior supraclavicular and axillary field, measuring 15×15 or 20×12 cm., depending on the patient's build, extends from just below the mastoid process to below the anterior axillary fold, permitting irradiating in continuity of the entire cervical chain, the supraclavicular, infraclavicular, and axillary nodes. The field is truncated at its lower medial border in order to minimise irradiation of the lung and, when necessary, the head of the humerus is shielded to avoid high-dose effects.

This group of nodes is virtually subcutaneous and within the 80 per cent isodose limit, with the exception of the axillary portion, which is deeper and thus necessitates the additional posterior field. The posterior axillary portal generally measures 10×8 cm. and is directly opposed to the lower section of the anterior supraclavicular field.

TREATMENT OF THE CHEST WALL

One widely adopted procedure for irradiation of the chest wall is the so-called tangential technique with an opposed pair of high-voltage beams at a glancing angle, designed to include the skin, subcutaneous tissues, and rib cage from the sternal border to the posterior axillary line, while taking in no more than a small anterior segment of lung tissue (15). Inherent in this method, however, are certain serious physical limitations, precluding homogeneous irradiation of the treated area. The region contains a heterogeneous complex of tissues, among which are skin, bone, and lung, with wide differences in density and mean atomic number. Furthermore, the contour varies irregularly in all directions, with a number of convexities and concavities in any one individual and extreme variations in shape from one patient to another. Since the edge of the beam is used, radial gradients from edge to center introduce a further error. These considerations, together with daily variation in

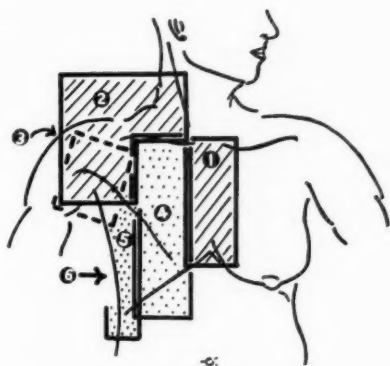


Fig. 1. Arrangement of fields in combined peripheral plus direct superficial irradiation technique.

angulation, the difficulty of ensuring true edge-to-edge opposition of the two beams, and the inconstant effect of the booster fields necessitated by the wider separation of opposed portals in obese patients combine to make accurate dosimetry impossible. In practice such cumulative errors in dosage may exceed 30 per cent (9, 43, 45).

An alternative chest-wall technique is the use of direct superficial therapy (low-voltage) portals (45, 46, 53). The effect of curvature of the chest can be overcome by using a number of smaller "patched-on" fields, compensating for edge effects either by deliberate overlapping of small margins (21) or by a moving-strip procedure (5). One such method, using three elongated (20×7 cm.) fields, contiguous with the high-voltage portals described, and allowing a 1-cm. overlap between adjacent fields, is shown in Figure 1. The quality of radiation for this method must be so chosen as to permit adequate treatment of a sufficient thickness of the chest wall, at the same time ensuring that the combined depth doses in the lung, where the axes of the three fields converge, remains within safe tolerance limits. A half-value layer of 2 to 4 mm. Al seems to meet this requirement, which is conveniently obtained at a potential of 135 kvp with filtration of 1 or 2 mm. Al, at a focus-skin distance of 25 cm. (see isodoses in Fig. 2). The method is readily reproducible, irrespective of the

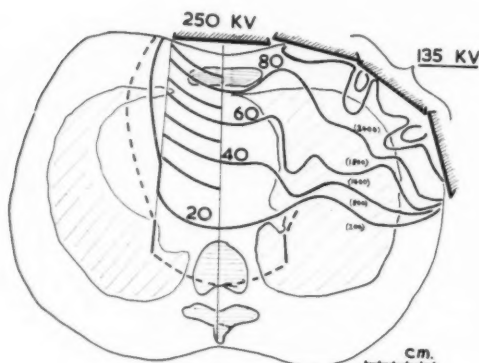


Fig. 2. Composite isodoses for combined peripheral and superficial irradiation technique. Figures in parentheses indicate actual absorbed dosage received in the lung.

patient's size or contour and eliminates all the inconsistencies and inaccuracies associated with the tangential technique. At the dosage used, no difficulties arise from the relatively heavily irradiated 1-cm. overlap strips, because of the high tolerance of narrow elongated skin fields (36). On the other hand, consideration of the composite isodoses in depth (Fig. 2) shows that a significant fraction of lung tissue (up to one-third of the lung when the right side is treated) receives a dose sufficient to induce minimal pneumonitic changes, with the risk of some residual fibrosis in certain cases.

A further method which has not been routinely adopted, due to the high integral dose, is a radium mould applied to the chest wall.

THE TIME-DOSE FACTOR

The clinical efficacy of any given dose of ionizing radiation is critically dependent upon the time over which such treatment is spread. Consequently it becomes necessary, in the treatment of breast cancer by irradiation, to consider the dosage and time factors simultaneously. Since there is little evidence in the radiological literature of any uniformity in practice, or any generally accepted time-dose routine for this disease, the required information can be obtained only through statistical processing of collected data, assuming empirical

time-dose functions of the type proposed by Strandqvist (61) and elaborated by Cohen (22), Andrews (4), and Du Sault (26). These authors agree that such data are best described by an iso-effect function of the type $D = E \cdot T^n$, where D is the physical absorbed dose; T is the number of daily fractions; E is a quantity specifying the radiosensitivity of the tumour, being the dose required to produce a standard effect, such as the median lethal dose (LD 50) or, more practically, the 90 per cent curative dose (LD 90), for a single short exposure; n is a "recovery exponent" which determines the degree to which prolongation of treatment time affects the required dose. If the parameters E and n can be determined, then an appropriate combination of dosage and time can be chosen to produce a desired end-result.

With this in view, all the relevant information on the radiosensitivity and recovery functions of human mammary cancer available up to the time of publication was collated (19, 21). An analysis of 60 patients treated in the Johannesburg Hospital with a variety of time-dose combinations prior to the adoption of any standard procedure in that institution showed that the median lethal dose for the tumour was $E = 1,270$ r (single exposure at 200 kv) and that the recovery exponent was of the order $n = 0.35$. Both these parameters were also estimated from collected published data independently, by the method of least squares, so as to derive the theoretical logarithmic regression of dose (D) on time (T), and hence to estimate the median curative dose (E) and the recovery exponent (n) in the iso-effect formula given. The result of this analysis indicated an LD 50 of $E = 1,200$ r and $n = 0.33$, in excellent agreement with the preceding estimates. Similarly, large recovery exponents of the order of $n = 0.34$ have also been reported for endometrial carcinoma by Costolow *et al.* (23). Du Sault (26) suggests that this factor may be characteristic of all glandular tissues, including those of the breast and alimentary and genital tracts.

Given that the median lethal dose, or LD

50, for this tumour corresponds to a value of $E = 1,270$, and the coefficient of variation among individual cases is of the order of 11 per cent (21), it follows from simple statistical theory that an adequate curative dose, or LD 90, can be attained if the LD 50 is exceeded by a factor equal to twice the coefficient of variation, say by 23 per cent. Thus the LD 90 would be given by $E = 1,500$. That is to say, it should be possible to eradicate the tumour in over 90 per cent of cases by a single exposure of orthovoltage roentgen rays to a tumour dose of 1,500 r or to the correspondingly larger doses required with fractionated procedures.

Some additional information has become available since this analysis was first published. Friedman and Pearlman (28) attempted to establish what they term the "corroborated lethal dose" for metastatic skin nodules irradiated over various periods. These authors assign, on the basis of a freehand graphical interpolation, an empirical "minimum tumour lethal dose" for breast cancer of 2,000 r at a single exposure and a corresponding recovery exponent of $n = 0.25$. Examination of their data, however, shows that this apparent discrepancy is not statistically significant, and that the findings could equally well be fitted by a curve originating at $E = 1,600$ with a slope of $n = 0.34$. Since the corroborated dose is, in fact, the LD 90, this result is in excellent agreement with our estimates. A further verification of these findings is given by the observations of Cochran *et al.* (16), who, on the basis of our estimated radiosensitivity of breast cancer, treated a series of patients with betatron photons in two daily fractions. Their reported effective dose was 2,500 r in two days, which corresponds to a single exposure of 2,000 r or, allowing for the difference in relative biological efficiency, a value of $E = 1,400$ at orthovoltage qualities.

DIFFERENTIAL RECOVERY

There is still no evidence, either in the foregoing analysis or in the available litera-

ture, of any favorable differential recovery on the part of mammary cancer as compared with normal tissues. The recovery exponent for breast cancer ($n = 0.34$) is practically identical with that estimated for normal skin ($n = 0.33$), so that, unlike epidermoid cancer ($n = 0.22$), the therapeutic ratio cannot increase with protracted courses of treatment. Although there may be other reasons for not giving the whole treatment in a very short time and other fractionation procedures capable of increasing the therapeutic ratio, there is no theoretical advantage, as far as the local reaction is concerned, in prolonged daily fractionation for breast cancer.

It appears, however, that factors other than dosage and overall time may have a significant influence upon the outcome of such treatment. Indeed, before any simple iso-effect function can be applied with confidence, it is necessary to consider at least three timing variables in addition to the overall treatment time. These include the intensity or dose-rate of the irradiation; whether the exposure is continuous or intermittent; and, in the latter case, the manner of fractionation; that is, the size, frequency, and spacing of individual exposures. If it is found that any of these variables affect the dose-dependence to a different degree in the tumour as compared with normal tissues, then some selective action or advantageous differential effect of radiation could be exploited in practice by a judicious choice of the appropriate factors.

Within the limits usually encountered in practice, and considered apart from associated changes in overall time, variation in dose-rate appears to have an insignificant effect upon the intensity of the reaction, the skin erythema reaction, for example, showing no perceptible differences attributable to changes in dose-rate over the whole range between 10 and 10,000 r per minute (41). Other studies have demonstrated a slightly greater effect with single exposures at high intensity (12, 35), but this effect diminishes rapidly as the number of fractions are increased (40).

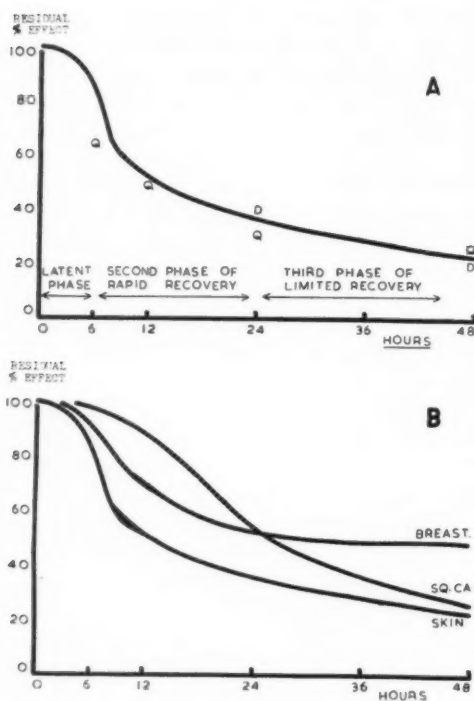


Fig. 3. A. Initial recovery curve for human skin as assessed up to forty-eight hours after a single exposure. Lettering refers to Duffy (25) and to Quimby and MacComb (55) respectively.

B. Three hypothetical variations in shape of the initial recovery curve which could account for observed differences in effect associated with different fractionation procedures in certain tumors.

With the procedures generally used in therapy, therefore, reactions are largely independent of dose-rate, and this factor can probably be discounted in practice. Similarly, differences between the effects of continuous protracted irradiation and intermittent exposure at sufficiently frequent intervals over the same total period also appear to be insignificant (44).

Variations in the fractionation scheme have, in general, a relatively slight effect upon biological reactions, compared with the overriding importance of the overall time in this respect. There is, however, strong indirect evidence that a differential effect attributable to this factor, as distinct from the overall time, does in fact exist and may significantly influence the result of irradiating certain tumours, including

human mammary cancer. The effect of varying the interval between treatments will accordingly be considered in more detail.

OPTIMAL INTERVAL BETWEEN TREATMENTS

The rate of recovery of human skin from the first and from subsequent doses of radiation given at various intervals has been estimated by studying the erythema reaction produced with different fractionation schemes. From the data originally reported by Duffy (25) and by Quimby and MacComb (55) on the effect of two equal fractions given at various intervals ranging from six to ninety-six hours apart, the degree of initial recovery can be assessed as a function of time. A composite recovery curve derived from these results is given in Figure 3, A. More recent investigations by Kepp (39) and by Du Sault (26) confirm the validity of this curve, at least in so far as its general shape is concerned. Among the significant features of the initial recovery curve of irradiated human skin are three distinct phases. First, there is a latent interval of five to six hours before any recovery commences, and any treatments given within this period appear to be fully cumulative, no matter how fractionated. This is followed by a more or less rapid depreciation in the residual effect, continuing for about forty-eight hours, after which the curve gradually merges with the third phase of slow recovery with partial cumulation over long periods.

It appears that the initial recovery of tumours differs somewhat from that of normal skin. This is shown by comparison of reactions in the case of standard daily fractionation procedures with those in clinical experiments in which the course is fractionated at intervals other than one day. There is evidence (63) of a favourable differential effect between skin and epidermoid cancer when this tumour is irradiated twice daily, while longer intervals between treatments, such as "alternate-day" or "twice-weekly" procedures, appear to give a favourable differential in the

therapy of breast cancer but not with epidermoid cancer (56). Du Sault has adduced some evidence for a critical interval between treatments at which differential effects are optimal (26).

The observed differential effects could be explained by differences in the initial phases of the recovery curves for the tumours and tissues concerned, as suggested in Figure 3,B. These curves are designed to show how a maximum differential could appear between skin and squamous cancer at twelve hours, and between skin and breast at forty-eight hours, to account for the observed responses reported by Van Roojen (63) and by Sambrook (56), respectively, and yet retain the general features of the triphasic initial skin recovery curve described.

If the functions postulated in Figure 3,B are even approximately correct, then it follows that the number of fractions, and not the overall time, would be a decisive factor in the radiation therapy of breast cancer, provided the interval between successive exposures was at least forty-eight hours. This conclusion is confirmed by many reports on the efficacy of widely spaced and repeated courses of treatment in this disease, as exemplified by the results of Berven (8), who obtained excellent control of the tumour with doses of 6,000 r delivered in three separate courses totaling 15 fractions with an overall period of sixty days, in contrast with Lenz's (42) failure to control the growth with 6,000 r delivered in 60 daily fractions. Similarly, data by Kaae (38) showed that 3,500 r, given in 20 fractions within one month, failed to reduce the incidence of chest-wall recurrences, while in the authors' present series, the same total dose given in the same overall time but with 10 alternate working-day fractions, was found most effective in this regard.

In practice, therefore, the optimal interval between treatments would be determined by the necessity of continuing individual fractions of suberythral magnitude until an adequate tumour dose had been delivered and spacing treatments so

that the overall time would be sufficient to ensure that this dose would not exceed the limits of skin tolerance. With a field diameter of the order of 20 cm. and allowance for a reasonable latitude between skin tolerance and tumour-lethal doses, the shortest adequate regime appears to be 10 fractions of 350 r each, spread over four weeks, any one field receiving treatment on alternate working days only (three days one week and two the next), as shown in Figure 4. This curve was derived by assuming a value of $n = 0.33$ for both skin and tumour, and accepting the initial recovery functions postulated in Figure 3,B.

From the foregoing considerations it appears that at least three such optimal procedures could be derived. One is the dose of 3,500 r in the 10 fractions described, which gives a theoretical cure-rate of over 90 per cent, yet remains well within the skin tolerance limits for the large fields required. With somewhat smaller fields, the shortest practicable course would consist of suberythral fractions, each of about 500 r. In order to be both safe and effective, this would have to be continued to a total tumour dose of 3,000 r delivered over a period of not less than sixteen days, that is in 6 twice-weekly fractions. The third alternative is a single exposure of about 1,500 r, which would be well tolerated by fields under 10 cm. in diameter or by elongated portals of equivalent area. The analogy between this series of optimal dose-time combinations, and that derived by von Essen (64) for epidermoid cancer is noteworthy.

OPTIMAL DOSAGE AND PERMISSIBLE HETEROGENEITY

A rigorous algebraic method for computing therapeutic ratios and optimal dosage in this type of problem has been devised by Cohen (20), who used the composite iso-effect function for skin and tumour

$$D = E.T^n.L^{-n/q}$$

where D , E , T , and n represent the factors described in previous paragraphs, L is the field size in decimeters, q is the diffusion

exponent, and η is the relative biological efficiency based on the high-energy or radium standard.

Although our dosimetric analysis has thus far been expressed in roentgens, D should ideally be given in terms of the absorbed dose in rads. Comparisons of the substandard dosimeters used in the Radiation Therapy Department of the Johannesburg General Hospital with those of the National Physical Laboratories at Pretoria and in the United Kingdom, as well as with chambers recently calibrated by the National Bureau of Standards in the United States, have shown our older "roentgen," upon which previous estimates of tissue dose were based, to be a "strong" one, numerically equivalent to almost exactly 1.00 rad. This propitious circumstance permits us to interpret previously established parameters in terms of rads without significant loss of accuracy. The optimal dosage factors given below are expressed in terms of true absorbed dose in rads and are based upon the best estimates of the relevant parameters currently available. The numerical values quoted derive from Cohen's collected data (20).

With the optimal time-factor of 10 fractions over four weeks, the skin or tissue tolerance limit is derived by substituting in the formula the values: $E_s = 3,000$; $T_s =$ twenty-five days; $L_s = 2.5$ dm.; $n_s = q_s = 0.33$; and η for 250-kv roentgen rays = 1.5. The maximum or tolerance dose is found to be $D_s = 4,300$ rads. Similarly, for the tumour lethal dose (LD 90), $E_t = 2,300$; $T_t = 10$ fractions (irrespective of elapsed time); L_t is immaterial since $q_t = 0$; $n_t = 0.34$; η is still 1.5; hence the minimum tumour dose is $D_t = 3,300$ rads. The margin of safety or therapeutic ratio is thus substantial, permitting a heterogeneity factor D_s/D_t of 1.3. The empirical given dose of 3,500 rads would, under the technical conditions to be described, fall well within these limits. The chest wall is often treated, for reasons described below, with superficial therapy fields at 135 kv, h.v.l. 3 mm. Al, and $\eta = 2$, under which conditions D_s

= 3,200 and $D_t = 2,500$, and the optimal given dose is taken at 2,700 rads.

The techniques by which the foregoing time, dose, and heterogeneity combinations are achieved in practice will be elucidated in the following section.

PRACTICAL TECHNIQUES

In the light of the foregoing considerations, it appears that five distinct procedures are required to cover the full range of cases which may be referred for irradiation. The following policy, by which any given patient may be allocated the appropriate treatment, has been adopted in our Radiation Therapy Department and will be the basis of the statistical review to be presented. The results of treatment with the various methods described will be tabulated and analysed in a later section of this report.

I. High-Voltage Irradiation of the Three Peripheral Fields Combined with Direct Superficial Therapy to the Chest Wall: The arrangement of fields for this procedure has been described previously, and is illustrated in Figure 1. The 3 peripheral fields are treated with 350 rads on alternate days to a total of 3,500 rads in 10 fractions over four weeks, while the superficial fields, treated with 300 rads on the intervening days, receive a total of 2,700 rads in 9 fractions over the same period. Skin reactions to these two dose levels are identical, thus proving that our estimated relative biological effectiveness for the low-voltage radiation ($\eta = 2$) is substantially correct. This procedure is used routinely on all suitable postoperative patients, including those late cases in which local mastectomy is technically feasible.

II. High-Voltage Irradiation of the Peripheral Fields with Tangential Beams to the Chest Wall: In this technique the chest wall is irradiated through a pair of opposed tangential portals (with bolus) as described, with the addition of a central booster field when necessary (2). The peripheral and tangential portals are treated alternately, each area receiving 3,500 rads in 10 fractions over four weeks. This method was

used in all cases treated from 1950 to 1952 and is particularly suited to those post-operative patients in whom obesity or excessive swelling or induration of skin flaps renders the chest wall too thick for superficial therapy. The technique is also appropriate for the radical treatment of inoperable patients. It is valuable in many locally advanced cases, in which it often affords the best palliation.

3,000 rads in 6 twice-weekly fractions, each of 500 rads.

V. Palliative Therapy to Isolated Metastases: With reasonably localised metastases in bone or soft tissue, each lesion is irradiated through one or more fields large enough to include the affected areas. With small or elongated fields, single exposures of high-voltage radiation to doses of taking not more than 1,500 rads on the

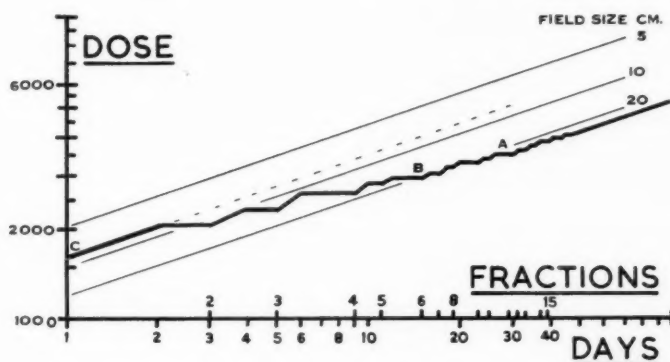


Fig. 4. Dose-time relationship. Heavy line shows LD 90 for mammary cancer treated on alternate days. Thin lines indicate skin tolerance doses for corresponding periods. A, B, and C represent the three optimal-dosage points described.

III. High-Voltage Peripheral Fields Alone: In the case of patients subjected to very radical operations, in whom it is felt that the thin chest wall cannot tolerate the full standard dosage, treatment is directed to the peripheral fields alone on alternate working days to a total dose of 3,500 rads in 10 fractions over four weeks. The untreated chest wall is observed on a careful follow-up, and further irradiation is considered only if obvious or suspicious recurrent tumour nodules appear.

IV. Radical Irradiation of Small Volumes: In the case of limited volumes requiring radical dosage, such as a small primary tumour in a frail or elderly subject having a short life expectancy, or a localised extension or recurrence within or beyond the treated area, a technique of somewhat shorter duration, corresponding to point B in Figure 4, may be used. This consists of high-voltage radiation to one or more single fields, to a total approaching

skin have been found safe and effective, usually resulting in complete and permanent relief of pain in the treated area, eventual recalcification of bone defects, and a moderate erythematous skin reaction.

REACTIONS, RISKS, AND COMPLICATIONS

As one would anticipate from the iso-effect lines of Figure 4 and the time-dose data discussed previously, the skin reactions have been almost identical with all the techniques described, consisting generally of little more than a marked erythema (second degree reaction), followed by superficial desquamation and pigmentation in the irradiated area. The only exceptions are in the case of the axilla and in the narrow overlapping margins between contiguous fields, where dosage is somewhat higher than average, resulting in an occasional moderate exudative reaction. These high-dosage zones have always healed uneventfully, leaving no more than



Fig. 5. Healing phase of the dry desquamative reaction attained after irradiation with combined peripheral (250 kv; 3,500 rads) and superficial (135 kv; 2,700 rads) technique. Note identical intensity of erythema and pigmentation in all areas, except for pale zones at overlapping edges of contiguous fields. (Photograph by courtesy of Dr. P. Keen).

some localised telangiectasia. We have observed no skin necrosis in patients treated by the standard procedures described, in contrast with our previous "all-fields-daily" regime (21), in which the same total dosage resulted in more severe reactions, with a small but significant incidence of chest-wall necrosis.

Apart from occasional asymptomatic osteoporotic lesions of ribs underlying the treated areas, and a few cases of stiffness of the irradiated shoulder joint, there have been no severe musculoskeletal complications. Lymphoedema of the arm on the affected side was not infrequently encountered after the radical operation, but only rarely in patients who had not had axillary dissection. In 2 cases, the angiosarcoma classically associated with post-mastectomy lymphoedema (60) has developed.

The incidence of pneumonitis, with or without permanent residual fibrosis, appears to depend upon several factors, both clinical and physical. The composite isodoses within the lung substance indicate that with Technique I (Fig. 2) almost one-third of the right lung (substantially less of the left, receives a dose approaching 2,000 rads, which may be considered a borderline pneumonitis dose (14, 66). Published isodose data for the tangential technique reveal a similar situation (37,

45) and, although our results indicate a lower fibrosis rate with the high-voltage technique (Table VI), there was no obvious *a priori* reason to favour either procedure in this respect. Whether the small added risk to the lung is offset by the special advantages of this particular technique will be considered along with the tabulated results. There was no evidence of any cardiovascular damage attributable to the radiation (11, 37).

TABLE I: AGE DISTRIBUTION AND AGE-SPECIFIC INCIDENCE OF BREAST CANCER IN THE SOUTHERN TRANSVAAL REGION

Age in Decades	Female Population in Each Decade (%)	Number of Cases in Each Decade	Age-Specific Incidence*
0-9	22.03	0	..
10-19	17.15	2	4
20-29	15.36	6	14
30-39	14.62	55	135
40-49	12.34	104	303
50-59	8.38	122	522
60-69	5.98	118	706
70-79	3.14	51	581
80-89	.90	8	320
90-	.07	0	..
TOTAL	99.97	466†	164

* Frequency of tumours per million women per year; assuming 400,000 women at risk for the seven-year period under review.

† The 3 male patients have been excluded.

STATISTICAL REVIEW

The population from which our clinical sample is drawn consists of approximately 3,000,000 persons domiciled in the southern half of the Transvaal, of whom roughly one-third are of European (white) descent. This survey will be confined to the European section, which, in contrast to the African population, forms a reasonably stable and homogeneous group amenable to accurate anamnesis and rigorous follow-up control and hence is more likely to yield data comparable with statistics published from other centers. With allowance for those patients who were either irradiated elsewhere or treated by surgery or chemotherapy and hence were not referred for our appraisal, it appears that about 80 per cent of all cases of breast cancer arising in this segment of the population eventually reach our center. The sex ratio in the white

TABLE II: NUMBER OF CASES PRESENTING IN VARIOUS STAGES, NATURE OF TREATMENT RECEIVED, AND THE FIVE-YEAR SURVIVAL AND CURE RATES FOR THE YEARS 1949 TO 1955 INCLUSIVE

Year →	1949	1950	1951	1952	1953	1954	1955	Total
Cases presenting	90	58	61	53	58	67	82	469 (100%)
Number treated	88	49	55	51	52	64	73	432 (92.1%)
Stage								
Stage I	16	16	21	16	19	21	27	136 (29.0%)
Stage II	23	13	16	18	15	27	26	138 (29.4%)
Stage III	13	5	2	6	5	9	14	54 (11.5%)
Stage IV	5	14	10	13	19	8	14	83 (17.7%)
Unstaged	33	10	12	0	0	2	1	58 (12.4%)
Surgery								
Radical mastectomy	73	37	47	37	40	37	42	313 (66.7%)
Local mastectomy	10	9	3	8	8	21	28	87 (18.6%)
No mastectomy	7	12	11	8	10	9	12	69 (14.7%)
Irradiation								
Combined technique	0	0	20	26	20	26	34	126 (26.8%)
High-voltage tangential	5	32	5	6	8	7	10	73 (15.5%)
High-voltage peripheral	1	0	8	10	12	18	19	68 (14.5%)
Non-standard	82	17	22	9	12	13	10	165 (35.2%)
Not irradiated	2	9	6	2	6	3	9	37 (7.9%)
Survival								
Untraced (dead)	2	2	3	1	2	4	0	14 (3.0%)
Absolute survival	44	31	24	20	21	21	37	198 (42.2%)
Net survival rate	43	28	23	20	20	21	37	192 (44.4%)
Recurrence-free	36	23	22	16	17	18	31	163 (37.7%)
Untreated, alive	1	3	1	0	1	0	0	6 (1.2%)

population of this area is 49.6 per cent female, so that the population at risk may be taken as approximately 400,000 women (47).

Although our clinical material cannot be considered a wholly unselected sample in the statistical sense, the degree of selectivity is unlikely to affect our conclusions, which are based upon intradepartmental subdivisions rather than interhospital comparisons. The series reviewed consists of 469 white patients with breast cancer, 3 of them males, seen in the Radiation Therapy Department of the Johannesburg General Hospital between 1949 and 1955 inclusive, and followed through June 1960. All new cases seen, regardless of whether or not they were treated, are included. The 1949 group has a degree of selection, in that previously treated patients who were alive and on follow-up at that time, are included. Almost all the 1949 patients come into the non-standard treatment group (see Tables), which has been separated from the other "standard" procedures, giving some valuable comparative data. The five-year results for cases treated in 1955 are assessed as of June 1960.

TABULATED RESULTS

Table I furnishes a description of the age structure of the material under review, which may be necessary if comparisons are to be made with corresponding series in other countries. The proportion of the white female population in each decade of life (1951 census) is listed, together with the number of cases presenting in the corresponding decade. Thus the age-specific incidence of breast cancers arising each year per million women can be estimated and shown to be comparable to that in other countries (3). This rate increases steadily up to the seventh decade, after which there is the rapid fall-off characteristic of endocrine-dependent tumours (33).

Table II is designed to show the degree of consistency in material presenting over the whole period under review. Since various technical innovations were introduced at different times, it is important to ensure that there were no marked differences in staging or other uncontrolled factors likely to affect the outcome over that period. It will be noted that less radical operations were done in the later years, and that the radiation technique

TABLE III: FIVE-YEAR SURVIVAL RATES FOR EACH STAGE TREATED BY DIFFERENT IRRADIATION TECHNIQUES

Technique	Stage I		Stage II		Stage III		Stage IV		Untaged		Total	
	No. of Cases	(%)	No. of Cases	(%)	No. of Cases	(%)	No. of Cases	(%)	No. of Cases	(%)	No. of Cases	(%)
Peripheral fields + superficial irradiation of chest wall	55	73	46	28	13	(23)*	4	(25)*	8	(50)*	126	48.4
High-voltage peripheral + tangential fields	24	67	22	41	10	(0)*	8	(0)*	9	(56)*	73	41.1
High-voltage peripheral fields only	21	71	29	45	10	(50)*	7	(14)*	1	(100)*	68	51.5
All others (37 untreated cases included)	36	67	41	32	21	43	64	9	40	50	202	35.6
TOTAL (all techniques)	136	70	138	35	54	32	83	10	58	52	469	42.2

* Percentages in parentheses are based on small numbers of cases and are statistically insignificant.

changed from a preponderance of non-standard procedures in 1949, favouring the standard tangential method in 1950, to the combined procedure described, from 1951 onward. Of the 469 patients, 432 or 92 per cent were treated by some form of irradiation directed to the breast area. The remaining 37 cases are classified as untreated since they received no radiotherapy to the primary region, but had palliative irradiation for metastases or got no treatment other than chemotherapy after the initial interview.

Survival rates showed no significant changes during the period studied. Although the follow-up was a consistent 97 per cent throughout, it was not always possible to determine the precise cause of death in the fatal cases. It has been assumed, therefore, that all patients who have succumbed have died with cancer. No corrections have been made for the age distribution, mortality from other causes, or the small number of untreated patients, nor have any actuarial studies been made. The effect of these omissions is likely to be a virtual survival rate somewhat lower than the true figure. The overall absolute and net survival rates of 42 per cent and 44 per cent, respectively, are comparable with most other published series (59, 67).

Table III is an analysis of the absolute survival rates obtained with the various therapeutic techniques described, applied at different stages of the disease. The staging adopted is a clinical one, assessed before operation and following the Manchester classification (51). Most cases were seen only after some form of surgery had been done, and the stage given by the referring surgeon was then accepted. The three standard irradiation techniques have been considered separately, while all the non-standard procedures, both radical and palliative, have been collected into the fourth group. This "non-standard" group includes all patients receiving the "small-volume" and "palliative" procedures (Techniques IV and V respectively), as well as those patients on follow-up in 1949 who had been treated with a variety of

TABLE IV: LOCAL RECURRENCE RATES IN CHEST WALL AND REGIONAL NODES AFTER TREATMENT BY DIFFERENT IRRADIATION TECHNIQUES

Technique	Total Cases Treated	Recurrence in Chest Wall	Recurrence in Regional Nodes	Total Local Recurrence	Recurrence Rates in Five-Year Survivors
Peripheral fields + superficial irradiation of chest wall	126	8 (6%)	2 (2%)	9 (7%)	0/61 (0%)
High-voltage peripheral + tangential fields	73	3 (4%)	4 (5%)	4 (5%)	0/30 (0%)
High-voltage peripheral fields only	68	13 (19%)	3 (4%)	14 (21%)	4/35 (11%)
All others (only treated cases)	165	22 (13%)	7 (4%)	25 (15%)	6/65 (9%)
TOTAL (all techniques)	432*	46 (11%)	16 (4%)	52 (12%)	10/192 (5%)

* With exclusion of 37 untreated cases.

time-dose combinations, with a total range between 3,000 and 4,000 r delivered in 15 to 20 equal daily fractions. Since this last group contains a high proportion of Stage IV cases, no significance can be attached to its lower survival rate (35.6 per cent) as a whole, nor are the smaller differences between the three standard routines statistically significant. Similarly, there is no significant effect on survival attributable to differences in technique in any one stage, although the effect of differences in staging upon the survival rate is apparent. It must be concluded that, as far as the five-year survival rate is concerned, no particular radiotherapeutic technique has been shown to have any superior merit.

Table IV shows that, in contrast to survival rates *per se*, the local recurrence rate is markedly dependent upon the exact nature of the treatment given. As shown previously, the main object of radiation therapy in breast cancer is the prevention or control of local recurrence of the disease. The fact that the local recurrence rate is very much lower with either of the two standard chest-wall treatments (4 to 6 per cent) than when peripheral fields alone are treated (19 per cent), or non-standard techniques are used (13 per cent), proves the efficacy of the dose-time combination selected. Since the "peripheral" group was selected for early staging and ready operability, this observation is highly significant. In spite of its physical advantages, however, the low-voltage direct-field approach has not proved superior in

this respect. Recurrence in the peripheral lymph nodes is infrequent (4 per cent) and independent of the particular irradiation technique employed. The total proportion of patients with local recurrence in either situation is shown to be less than the sum of rates for each site, since one patient may have recurrence in both sites. This total serves to illustrate the overall efficiency of treatment in postoperative cases.

The contrast in results attributable to differences in technique is even more striking when the local recurrence rate among the five-year survivors is considered. As shown in the last column of Table IV, there were no local recurrences in 91 five-year survivors who had received therapy by one of the standard chest-wall techniques. The fiducial limits of this ratio (Poisson) suggest that the true recurrence rate cannot exceed 3 per cent. A similarly low rate among five-year survivors has been reported by McWhirter (personal communication). By contrast, the peripheral and non-standard procedures still give a recurrence rate of 9 to 11 per cent, which is comparable with many other published series. This suggests that radiotherapy in correct dosage can eradicate the tumour with certainty, except when the patient's general resistance has deteriorated to the point where widespread dissemination occurs.

The foregoing observation supports the concept of radiosensitivity of tumours as a function of host resistance (18). Adequate doses of radiation serve to reduce the

TABLE V: FIVE-YEAR SURVIVAL AND RECURRENCE RATES FOR DIFFERENT SURGICAL AND IRRADIATION PROCEDURES

Technique	Radical Mastectomy			Local Mastectomy			No Mastectomy			Total	
	Cases	Survival (%)	Recurrences (%)	Cases	Survival (%)	Recurrences (%)	Cases	Survival (%)	Recurrences (%)	Survival (%)	Recurrences (%)
Peripheral fields + superficial irradiation of chest wall	85	48	6	41	49	9	0	126	48.4
High-voltage peripheral + tangential fields	36	58	3	17	41	(7)*	20	15	10	73	41.1
High-voltage peripheral fields only	63	54	18	5	(20)*	(80)*	0	68	51.5
All others (treated cases)	109	48	9	21	33	24	35	17	11	165	39.4
No irradiation	20	15	...	3	0	...	14	(29)*	...	37	18.9
TOTAL (all techniques)	313	45.5	10.5	87	40.2	14.9	69	18.8	10.9	469	42.2
											11.1

* Percentages in parentheses are statistically insignificant.

tumour-cell population to a subcritical level (17) corresponding to the small dormant metastases whose growth is normally restrained by systemic immune mechanisms in the patient (32). When this resistance mechanism fails, both local recurrence and overt metastases make their appearance simultaneously.

It was of some interest to investigate the fate of those patients receiving treatment to the peripheral fields alone, who, when a local recurrence on the chest wall developed without distant metastases, were re-treated with a view to further salvage. Of 8 patients so re-treated, only 2 responded satisfactorily, the remaining 6 dying with uncontrolled local cancer within a year. The average survival was less than two years following the secondary treatment, proving that the peripheral technique permits continued tumour progression in many cases and is consequently an unsatisfactory procedure.

Table V shows the effect of differences in the surgical approach upon the survival and recurrence rates. Both the survival and local recurrence rates appear to be slightly better with radical mastectomy than with more limited operations, although the differences are not statistically significant. The best survival rates (54 to 58 per cent) are apparently given by the combination of radical mastectomy with high-voltage peripheral or tangential irradiation, but since most of these cases must have been in the early or operable stage, and particularly as the peripheral technique was used mainly after very radical operations on specially selected early cases, this figure cannot be considered significant.

One striking feature, however, is the very poor result obtained if both surgery and radiotherapy are conservative, that is, when local mastectomy is combined with limited or non-standard irradiation. Of the 26 cases in this category, there were only 8 (31 per cent) survivors, and, more significantly, there was a local recurrence rate of 31 per cent, which is substantially higher than that in any other category. From the rigorous statistical point of view,

TABLE VI: FREQUENCY OF PNEUMONITIS AND FIBROSIS AFTER VARIOUS IRRADIATION TECHNIQUES ASSESSED AT FIVE YEARS*

Technique	Patients Cured for Five Years			Patients Dead or Alive with Cancer			Total Patients		
	Cases Treated	Pneu- monitis (%)	Fibrosis (%)	Cases Treated	Pneu- monitis (%)	Fibrosis (%)	Cases Treated	Pneu- monitis (%)	Fibrosis (%)
Peripheral fields + super- ficial irradiation of chest wall	54	13	4	72	23	9	126	29	10
High-voltage peripheral + tangential fields	25	3	0	48	10	1	73	16	2>
High-voltage peripheral fields only	29	3	0	39	8	1	68	16	2>
TOTAL	108	18	4	159	26	7	267	22	5.6

* Analysis based on 267 patients treated, by one of the three definitive techniques, to standard dosage. Pneu-
monitis implies any radiological evidence of lung reaction. Fibrosis means persistent symptoms of cough or
dyspnoea associated with the radiological changes.

however, it appears that, provided a mastectomy is done and the chest wall as well as the peripheral nodes are adequately irradiated, there is no real difference in results obtained with radical, compared with simple mastectomy, nor is there any significant advantage in the superficial over the tangential approach in irradiating the chest wall.

Table VI shows the frequency of pneumonitis and fibrosis with various techniques. It appears that in a large proportion of cases, 22 per cent of our series of 267 patients receiving the standard radical dosage, some form of lung reaction develops following treatment. This was detected by radiographs taken at the follow-up clinic either routinely in asymptomatic patients or in response to some specific complaint such as cough.

The majority of these pneumonitic reactions are transient, less than 6 per cent (15 patients in all) having persistent symptoms associated with radiologic evidence of fibrosis either in the apex or hilar region of the lung on the affected side. Since in 11 of these widespread dissemination of the tumor, including intrapleural and pulmonary extension, subsequently occurred, the relative roles of radiation and of secondary cancer in producing the lung changes cannot be assessed (52). There were no cases of massive fibrosis evidenced by complete unilateral blackout except in association with disseminated cancer. If

only patients free of cancer for five years are considered, the final fibrosis rate is 4 per cent.

It is of some interest that the 4 cases of undisputed fibrosis occurred in patients who had received radiation by the direct superficial technique, but this finding is not statistically significant in view of the small numbers available for analysis. However, the weight of evidence in Table VI points to a slightly greater risk with the superficial technique, which may be offset by an apparent survival rate greater by 7 per cent (Tables III and V) when compared with the results obtained with the tangential approach. The isodoses in Figure 2 suggest that a direct superficial technique with a slightly lower kilovoltage or diminished filtration would eliminate this possible defect in an otherwise ideal procedure.

SUMMARY AND CONCLUSIONS

From the available literature it appears that the five-year survival rate in breast cancer, all stages combined, is generally determined at the outset by the probability of widespread dissemination. The end-result is consequently unaffected by differences in treatment policy, except in so far as local recurrence of the disease is concerned. A statistical analysis of 469 patients treated by a variety of surgical and radiotherapeutic procedures and followed for five years confirms this view

and indicates that in a proportion of patients surviving without metastases recurrent cancer in the regional nodes and chest wall will develop if adequate radiotherapy is not given to these areas.

The nature of the operation (local or radical mastectomy) has little if any influence on the outcome provided adequate irradiation is given to both the regional nodes and the chest wall. Inadequate radiotherapy or treatment limited to the peripheral nodes is associated with a high recurrence rate, particularly after local mastectomy. With radical operations, when treatment must be confined to the peripheral fields alone or otherwise limited, we have observed a high rate of irretrievable chest-wall recurrences.

In order to achieve significant reduction in the local recurrence rate, radiation therapy must be administered according to a dose-time combination of proved efficacy. We have found that 3,500 rads in 10 fractions over four weeks (h.v.l. 3 mm. Cu) is suitable for radical treatment to the primary site and regional nodes, or 2,700 rads to the chest wall in 9 fractions over the same period (h.v.l. 2 mm. Al). In the case of osseous metastases treated with small or elongated fields, single exposures of 1,500 rads each are uniformly effective.

The standard techniques (high-voltage tangential irradiation or treatment through direct superficial portals combined with peripheral fields to the regional nodes) result in few complications other than a low incidence (approaching four per cent) of pulmonary fibrosis, generally affecting the apical or hilar regions and giving minimal symptoms. The quality of radiation or the arrangement of the fields appears to be relatively unimportant provided correct dosage is received by the whole affected area, in which case the recurrence rate among patients free of distant metastases is virtually zero.

NOTE: The success of the follow-up survey, without which this work could not have been completed, was entirely due to the efforts of Mrs. S. Wulfsohn, Social Worker to the Department. We are indebted

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REFERENCES

1. ACKERMAN, L. V.: An Evaluation of the Treatment of Cancer of the Breast at the University of Edinburgh (Scotland), under the Direction of Dr. Robert McWhirter. *Cancer* 8: 883-887, September-October 1955.
2. ALLCHIN, F. M., AND WILSON, C. W.: The Irradiation Treatment of Carcinoma of the Breast. *Brit. J. Radiol.* 21: 406-413, August 1948.
3. American Cancer Society (Statistics Department): Vital Statistics of the United States 1940. New York.
4. ANDREWS, J. R.: Radiation Therapy: A General Theory. *Am. J. Roentgenol.* 77: 531-539, March 1957.
5. BATLEY, F., AND HOLLOWAY, A. F.: Moving-Strip Technique in the Roentgen Treatment of Carcinoma of the Breast. *Am. J. Roentgenol.* 83: 532-537, March 1960.
6. BENNINGHOFF, D., AND TSIEN, K. C.: Treatment and Survival in Breast Cancer: A Review of Results. *Brit. J. Radiol.* 32: 450-454, July 1959.
7. BERVEN, E.: Treatment and Results in Cancer of the Breast. *Am. J. Roentgenol.* 62: 320-325, September 1949.
8. BERVEN, E.: Die Strahlenbehandlung des Mammakarzinoms. *Fortschr. a.d. Geb. d. Röntgenstrahlen (Sonderhft.)* 75: 10-25, December 1951.
9. BINKS, C., AND SHERRIFF, E. V.: The Measurement of Skin Dose with Particular Reference to Post-Operative Treatment of Carcinoma of Breast. *Brit. J. Radiol.* 27: 283-288, May 1954.
10. BYRD, B. F., JR., BURCH, J. C., STEPHENSON, S. E., JR., AND NELSON, I. A.: The Effect on Survival of Certain Variables in Breast Cancer. *Ann. Surg.* 149: 807-812, June 1959.
11. CATTERALL, M.: The Effect of Radiation upon the Heart. *Brit. J. Radiol.* 33: 159-164, March 1960.
12. CHAUL, H., WACHSMANN, F., AND ROSENBERGER, H.: Über den Einfluss der Protrahierung in der Strahlentherapie. *Strahlentherapie* 76: 224-259, 1947.
13. CHOPPING, P. T.: The Relationship Between Dosage Level and the Incidence of Recurrence in Post-Operative Irradiation for Carcinoma of the Breast. *Brit. J. Radiol.* 24: 401-402, July 1951.
14. CHU, F. C. H., PHILLIPS, R., NICKSON, J. J., AND MCPHIE, J. G.: Pneumonitis Following Radiation Therapy of Cancer of the Breast by Tangential Technique. *Radiology* 64: 642-653, May 1955.
15. CLARKE, K. H.: A System of Dosage Estimation for the Tangential Irradiation of the Breast without Bolus. *Brit. J. Radiol.* 23: 593-597, October 1950.
16. COCHRAN, D. Q., HOLTZ, S., AND POWERS, W. E.: The Rapid Palliative Treatment of Breast Carcinoma. A Preliminary Report. *Am. J. Roentgenol.* 81: 479-484, March 1959.
17. COHEN, A., AND COHEN, L.: Estimation of the Cellular Lethal Dose and the Critical Cell Number for

- A. Elliott, advice on the medical Dr. K. F. to hospital research
- the C3H Mouse Mammary Carcinoma from Radiosensitivity Studies in Vivo. *Nature*, London **185**: 262-263, Jan. 23, 1960.
18. COHEN, L., AND COHEN, A.: Radiosensitivity as a Function of Antigenic Equivocation. *Nature*, London **183**: 692-693, March 7, 1959.
19. COHEN, L.: Cancer of the Breast: Scope of Irradiation. *South African M. J.* **24**: 276-280, April 15, 1950; 565-568, July 15, 1950.
20. COHEN, L.: The Statistical Prognosis in Radiation Therapy. A Study of Optimal Dosage in Relation to Physical and Biologic Parameters for Epidermoid Cancer. *Am. J. Roentgenol.* **84**: 741-753, October 1960.
21. COHEN, L., AND SHAPIRO, M. P.: Radiotherapy in Breast Cancer. *Brit. J. Radiol.* **25**: 636-645, December 1952.
22. COHEN, L.: Estimation of Biological Dosage Factors in Clinical Radiotherapy. *Brit. J. Cancer* **5**: 180-194, June 1951.
23. COSTLOW, W. E., NOLAN, J. F., BUDENZ, G. C., AND DU SAULT, L.: Radiation Treatment of Carcinoma of the Corpus Uteri. *Am. J. Roentgenol.* **71**: 669-673, April 1954.
24. DALAND, E. M.: Untreated Cancer of the Breast. *Surg., Gynec. & Obst.* **44**: 264-268, February 1927.
25. DUFFY, J. J., McNATTIN, R. F., COPELAND, M. M., AND QUIMBY, E. H.: The Relative Effects Produced by 200 kv. Roentgen Rays, 700 kv. Roentgen Rays, and Gamma Rays. V. Comparison Based on the Production of Erythema in Human Skin. *Am. J. Roentgenol.* **29**: 343-345, March 1933.
26. DU SAULT, L. A.: Time-Dose Relationships. *Am. J. Roentgenol.* **75**: 597-606, March 1956.
27. EDSMYR, F., AND WALSTAM, R.: Method for Irradiation of Parasternal Lymph-Node Metastases. *Acta radiol.* **51**: 308-320, April 1959.
28. FRIEDMAN, M., AND PEARLMAN, A. W.: Time-Dose Relationship in Irradiation of Recurrent Cancer of the Breast: Iso-Effect Curve and Tumor Lethal Dose. *Am. J. Roentgenol.* **73**: 986-998, June 1955.
29. GARLAND, L. H.: The Rationale and Results of Simple Mastectomy Plus Radiotherapy in Primary Cancer of the Breast. *Am. J. Roentgenol.* **72**: 923-941, December 1954.
30. GATCH, W. D., AND CULBERTSON, C. G.: Theories on the Treatment of Breast Cancer and Observations on the Natural Course. *Ann. Surg.* **135**: 775-781, June 1952.
31. HAAGENSEN, C. D.: Carcinoma of the Breast. *J.A.M.A.* **138**: 279-292, Sept. 25, 1948.
32. HADFIELD, G.: The Dormant Cancer Cell. *Brit. M. J.* **2**: 607-610, Sept. 11, 1954.
33. HADFIELD, J.: The Effect of Hormone Deprivation upon Breast Cancer. *Ann. Roy. Coll. Surgeons (England)* **25**: 1-19, July 1959.
34. HAYBITTLE, J. L.: The Estimation of the Proportion of Patients Cured After Treatment for Cancer of the Breast. *Brit. J. Radiol.* **32**: 725-733, November 1959.
35. HOLTUSEN, H.: Vergleichende Untersuchungen über die Wirkung von Röntgen- und Radiumstrahlen. *Strahlentherapie* **46**: 273-288, 1933.
36. JOLLES, B., AND MITCHELL, R. G.: Optimal Skin Tolerance Dose Levels. *Brit. J. Radiol.* **20**: 405-409, October 1947.
37. JONES, A., AND WEDGWOOD, J.: Effects of Radiations on the Heart. *Brit. J. Radiol.* **33**: 138-158, March 1960.
38. KAAE, S.: Radiotherapy in Cancer of the Breast. *Acta radiol., Suppl.* **98**, 1952.
39. KEPP, R. K.: Der Erholungsablauf in der Haut nach Röntgenbestrahlung. *Strahlentherapie* **78**: 273-276, 1948.
40. KEPP, R. K., AND SEYFARTH, L.: Die Beeinflussung der Hautreaktion durch längere Bestrahlungspausen bei fraktionierte Röntgenbestrahlung. *Strahlentherapie* **76**: 573-583, 1947.
41. LAHM, W.: Über Radiumdosierung. *Strahlentherapie* **68**: 206-220, 1940.
42. LENZ, M.: Tumor Dosage and Results in Roentgen Therapy of Cancer of the Breast. *Am. J. Roentgenol.* **56**: 67-74, July 1946.
43. LOCHMAN, D. J.: Dosage in Tangential Radiation Therapy of the Postoperative Breast Portal. *Am. J. Roentgenol.* **73**: 803-812, May 1955.
44. McWHIRTER, R.: Radiosensitivity in Relation to the Time Intensity Factor. *Brit. J. Radiol.* **9**: 287-299, May 1936.
45. MEURK, M. L., AND CHU, F. C. H.: Dose Distribution with Four Radiation Technics for Carcinoma of the Breast. *Radiology* **73**: 607-617, October 1959.
46. MILLER, M. W., AND PENDERGRASS, E. P.: Some Observations Concerned with Carcinoma of the Breast. Part I. *Am. J. Roentgenol.* **72**: 263-270, August 1954.
47. The Official Year Book of the Union of South Africa, 1954-1955. Based on the Census of 1951.
48. OLIVER, D. R., AND SUGARBAKER, E. D.: The Significances of Skin Recurrences Following Radical Mastectomy. *Surg., Gynec. & Obst.* **85**: 360-367, September 1947.
49. PARK, W. W., AND LEES, J. C.: The Absolute Curability of Cancer of the Breast. *Surg., Gynec. & Obst.* **93**: 129-152, August 1951.
50. PATERSON, R., AND RUSSELL, M. H.: Clinical Trials in Malignant Disease. Part III: Breast Cancer: Evaluation of Post-Operative Radiotherapy. *J. Fac. Radiologists* **10**: 175-180, October 1959.
51. PATERSON, R.: The Treatment of Malignant Disease by Radium and X-rays. London, Edward Arnold and Co., 1948, p. 309.
52. PENDERGRASS, E. P., AND WHITE, G.: Pulmonary Metastases and Pneumonitis Following Radiation Therapy for Cancer of the Breast. *Am. J. Roentgenol.* **50**: 491-498, October 1943.
53. PFAHLER, G. E., AND KEEFER, G. P.: Object, Value and Technique of Preoperative and Postoperative X-Ray Treatment in Carcinoma of the Breast. *Surg., Gynec. & Obst.* **85**: 35-45, July 1947.
54. PHILLIPS, A. J.: A Comparison of Treated and Untreated Cases of Cancer of the Breast. *Brit. J. Cancer* **13**: 20-25, March 1959.
55. QUIMBY, E. H., AND MACCOMB, W. S.: Further Studies on the Rate of Recovery of Human Skin from the Effects of Roentgen- and Gamma-Ray Irradiation. *Radiology* **29**: 305-312, September 1937.
56. SAMBROOK, D. K., THACKRAY, A. C., AND WOODYATT, P. B.: Comparative Study of Radiotherapy Techniques. *Brit. J. Cancer* **4**: 63-76, March 1950.
57. SHIMKIN, M. B., LUCIA, E. L., STONE, R. S., AND BELL, H. G.: Cancer of the Breast: Analysis of Frequency, Distribution, and Mortality at University of California Hospital, 1918 to 1947, Inclusive. *Surg., Gynec. & Obst.* **94**: 645-661, June 1952.
58. SMITHERS, D. W.: Cancer of the Breast. A Study of Short Survival in Early Cases and of Long Survival in Advanced Cases. *Am. J. Roentgenol.* **80**: 740-758, November 1958.
59. SMITHERS, D. W., RIGBY-JONES, P., GALTON, D. A. G., AND PAYNE, P. M.: Cancer of the Breast. A Review. *Brit. J. Radiol., Suppl.* **4**, 1952.
60. STEWART, F. W., AND TREVES, N.: Lymphangiosarcoma in Postmastectomy Lymphedema; Report of 6 Cases in Elephantiasis Chirurgica. *Cancer* **1**: 64-81, May 1948.
61. STRANDQVIST, M.: Studien über die kumulative Wirkung der Röntgenstrahlen bei Fraktionierung. *Acta radiol., Suppl.* **53**, 1944.
62. TREVES, N., AND HOLLEB, A. I.: A Report of

549 Cases of Breast Cancer in Women 35 Years of Age or Younger. *Surg., Gynec. & Obst.* **107**: 271-283, September 1958.

63. VAN ROOJEN, J.: An Experimental Clinical Series in the X-ray Treatment of Epitheliomata. *Clin. Proc. (Cape Town)*, Suppl. 6, 1947.

64. VON ESSEN, C. F.: Roentgen Therapy of Skin and Lip Carcinoma: Factors Influencing Success and Failure. *Am. J. Roentgenol.* **83**: 556-570, March 1960.

65. WADE, P.: Untreated Carcinoma of the Breast: Comparison with Results of Treatment of Advanced

Breast Carcinoma. *Brit. J. Radiol.* **19**: 272-280, July 1946.

66. WHITFIELD, A. G. W., BOND, W. H., AND ARNOTT, W. M.: Radiation Reactions in Lung. *Quart. J. Med.* **25**: 67-86, January 1956.

67. WINDEYER, B. W., SMITHERS, D. W., AND CARLING, E. R.: Cancer of the Breast. [In] *British Practice in Radiotherapy*, edited by Carling *et al.* London, Butterworth and Co., Ltd., 1955, p. 147.

68. WYARD, S.: The Natural Duration of Cancer. *Brit. M. J.* **1**: 206-207, Jan. 31, 1925.

SUMMARIO IN INTERLINGUA

Therapia Radiational in Cancere Mammari: Combination Optimal de Factores Technic e Analyse del Resultatos Quinquenne

Ab le disponibile litteratura il pare que le superviventia quinquenne in cancro mammari de omne le stadios combinate es determinate generalmente ab le initio per le probabilitate de un extense disseminacion. Per consequente, le ultime resultato non es afficite per differentias del tactica therapeutic, excepte in tanto que recurrentias local es concernite. Un analyse statistic de 469 patientes tractate per un varietate de methodos chirurgic e radiotherapeutic e tenite sub observation durante cinque annos tende a confirmar ille vista.

Le natura del operation (mastectomia local o radical) ha pauc o nulle influencia super le ultime resultato, providite que un adequate irradiation es applicate tanto al nodos regional como etiam al pariete thoracic. Inadequate irradiation o un therapia limitate al nodos peripheric es associate con un alte incidentia de recurrentias, particularmente post mastectomia local. In operationes radical, quando le radiotherapia debe esser restringite al campos peripheric o es alteremente limitate, un elevate incidentia de irreparable recurrentias in le parietes thoracic esseva notate.

Pro effectuar un significative reduction del incidentia de recurrentias local, le radiation debe esser administrate secundo un plano de dosages e tempores de provate efficacia. Le autores ha trovate que 3,500 rad in 10 fractiones in le curso de quatro septimanas es appropriate pro le tractamento radical del sito primari e del nodos regional, o 2,700 rad al pariete thoracic in 9 fractiones intra le mesme periodo. In le caso de metastases ossee tractate con micre o elongate campos, expositiones solitari de 1,500 rad cata un es uniformemente efficace.

Le technicas standard (alte voltage tangential o directe portas superficial combinate con campos peripheric orientate contra le nodos regional) resulta in pauc complicationes a parte le basse incidentia de minus que 4 pro cento de fibrosis pulmonar afficiente generalmente le regiones apical o hilar e producente symptomas minimal. Le qualitate del radiation o le arrangiamento del campos pare esser relativamente pauc importante, providite que le correcte dosage es recipite per le integre area afficite. Allora le incidentia de recurrentias in patientes sin metastases distante es practicamente zero.

Hodgkin's Disease in Bone¹

IVAN S. FUCILLA, M.D., and ANNA HAMANN, M.D.

HODGKIN'S DISEASE is not exclusively a disease of the lymphatic system. Involvement of every organ system including the skeleton has been reported. The present discussion of Hodgkin's disease in bone is based on a review of the literature and a study of 94 previously unreported cases from the Veterans Administration Research Hospital, Chicago, and the Evanston Hospital (Evanston, Ill.) of which 11 showed osseous involvement. Askanazy (2) described the pathologic aspects of osseous involvement in 1920, some twenty years after the clear definition of Hodgkin's disease as an entity by Reed and Sternberg. Grossman and Weis (6) first recorded the radiographic features of the bony lesions in 1922.

INCIDENCE

The reported incidence of Hodgkin's disease in bone varies widely with the diagnostic criteria. A distinction must be made between medullary and cortical lesions. In the spongiosa the disease may be widespread without giving rise to symptoms or radiographic signs. The true incidence cannot be determined because of the limitations of the average post-mortem examination. The more diligent the search of the bone marrow, the greater the apparent incidence (13). Ewing (5) believed that it approached 100 per cent in patients dying of the disease. Only when there is extensive destruction or sclerosis are the lesions discoverable radiographically. Cortical involvement is more readily detectable; radiographic evidence may be found antemortem in approximately 15 per cent of all cases of Hodgkin's disease (Table I), and Uehlinger (14) states that in an additional 10 per cent cortical lesions will be discovered only at autopsy.

The mean age of occurrence of Hodgkin's

TABLE I: REPORTED SERIES OF HODGKIN'S DISEASE IN BONE

	Cases re-ported	Cases with Bone Lesions	Incidence of Bone Involvement (%)
Dresser and Spencer	149	16	10.7
Craver and Cope-land	172	27	15.7
Uehlinger	50	17	34.0
Vieta <i>et al.</i>	257	38	14.8
Fucilla and Hamann	94	11	11.7
TOTAL	722	109	15.1

disease is the fourth decade, and the peak incidence is in the third decade (8, 14, 15). These data correspond closely to cases with bone involvement. Although Uehlinger states that osseous lesions are a late and prognostically grave sign, the work of Vieta, Friedell, and Craver (15) and the new cases reviewed here do not substantiate this conclusion. Bone involvement occurs throughout the course of the disease, and its appearance does not affect the prognosis significantly. In this respect Hodgkin's disease differs from most metastatic tumors. The sex ratio is approximately equal.

SIGNS AND SYMPTOMS

Hodgkin's disease in cortical bone usually gives some indication of its presence, although large lesions are often found which have produced no signs or symptoms. The most common manifestation is localized pain. This may be intermittent or persistent and may occur in any phase of the disease. Negative radiographs may obscure its origin. Jackson and Parker (8) found that in 13 per cent of their cases symptoms were present for two to twelve months before positive radiographic findings were obtained. Occasionally pain without significant adenopathy directs attention to the disease. Tenderness to

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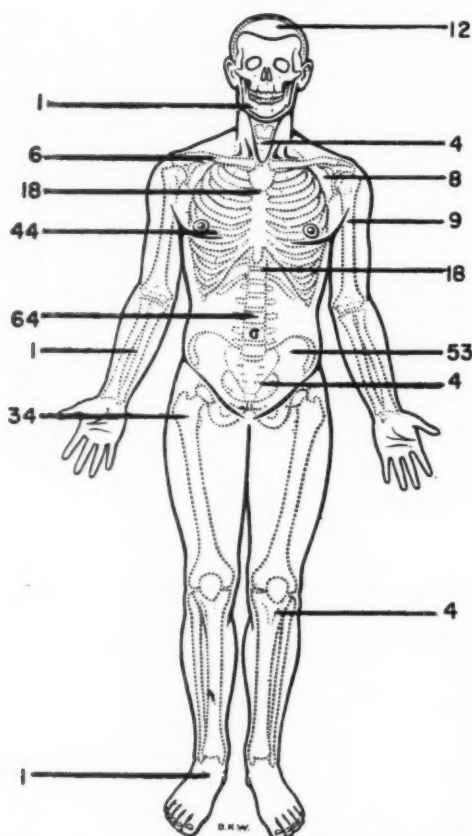


Fig. 1. The distribution of 284 lesions in 115 cases of Hodgkin's disease with bone involvement (collected from three series: Dresser and Spencer, Vieta *et al.*, and the authors).

pressure is a reliable sign and indicates bone destruction (3, 15); unfortunately, however, this sign is infrequent because of the inaccessibility of the involved bones. A mass or swelling is often found with bone destruction, particularly in the ribs and sternum. Neurologic deficits may occur as a result of vertebral collapse or pressure or invasion of the cord by contiguous disease.

The systemic symptoms and hematologic findings are substantially the same as in patients without detectable bone lesions. All of the new cases presented here had been treated both by x-rays and chemotherapy. A leukocytosis was frequently present initially, and a leukopenia after

treatment. The majority of the patients had a secondary anemia that could not be explained on the basis of bone marrow replacement alone. Sternal punctures do not help in the diagnosis for the following reasons: (a) the sternum is not always involved; (b) the lesions may be small; (c) the lesions are firmer than the surrounding marrow and are not easily aspirated (10, 15). The serum alkaline phosphatase level appears to have some diagnostic value. In the absence of liver disease, an elevated level strongly suggests bone involvement, although it does not indicate the location or degree. It is significant even in the absence of positive radiographic findings (1).

PATHOLOGY

There is nothing characteristic in the gross pathologic appearance of Hodgkin's disease in bone. The lesions vary from microscopic foci to large gray-white or yellow-white nodules in contrast to the darker marrow tissue. Histologically, the lesions show the same range of cellular variation as in non-osseous tissue (8). There is a diffuse hyperplasia with varying proportions of endothelial cells, endothelial giant cells, large and small lymphocytes, plasma cells, and eosinophils. The diagnostic feature is the Reed-Sternberg cell, a cell 12 to 40 microns in diameter, with an irregular nucleus, dense chromatin, and large nucleoli.

SPREAD

Hodgkin's disease spreads by two routes: by contiguity and hematogenously. The disease has great locally invasive and destructive capabilities (1, 5). Granulomatous masses frequently invade bones contiguous to the node-bearing areas, *i.e.*, the spine, pelvis, sternum, ribs, and the inner halves of the clavicles (13). Passage through the cortex is facilitated by its fenestration. In the medullary portion the granulomatous tissue may spread widely without causing apparent destruction. Lesions involving the cortex cause changes that can be detected radiographi-

ically early in their course. It is to these changes that most of the literature refers. Scattered lesions not related to nodal areas are considered to be of hematogenous origin. In common with other metastatic tumors these occur almost exclusively in the red bone marrow (16). The distribution in three series, including the authors', is shown in Figure 1. Anemia causing compensatory erythropoiesis may alter the distribution of the red marrow and account for unusual sites of metastasis. Hematogenous lesions are usually small and asymptomatic. Willis (16) rejects the theories of Handley (7) and Kolodny (9) concerning metastasis of tumors in general to bone through the lymphatic system, and injection studies have failed to demonstrate any lymphatics in bone. It is theoretically possible for Hodgkin's disease to arise primarily in bone, but this has not been conclusively demonstrated.

RADIOGRAPHIC FINDINGS

The most common sites of radiographically apparent lesions are the pelvis, particularly near the sacroiliac joints, the vertebral bodies, the sternum, the proximal halves of the clavicles, and the femurs. Hodgkin's disease of bone presents no pathognomonic radiographic findings. Only by histologic examination may the diagnosis be definitely established. In a proved case, however, osseous lesions should be regarded presumptively as manifestations of the primary disease. Occasionally bone involvement is found before the diagnosis has been established. Therefore, Hodgkin's disease should be considered in the presence of any bone lesion of obscure origin.

Hodgkin's disease in bone is predominantly osteolytic, with areas of osteosclerosis confined to the margins of smaller lesions or interspersed within the larger ones. Next in frequency, but considerably less common, is the pure osteolytic type. The destruction is often accompanied by expansion, particularly when involving the ribs or sternum. Pure osteoblastic involvement is rare and usually is seen only

in the vertebral bodies. Periosteal new bone formation is not common and, when it does occur, is minimal. Some spicule formation occasionally may be found, producing an appearance similar to osteogenic sarcoma (11). Multiple lesions are the rule, and any or all of the types of involvement described above may be found in one patient.

Radiographically, the maximum incidence of bone involvement is in the upper lumbar and lower cervical spine, corresponding to the prevertebral nodal areas (4, 13, 14, 15). The earliest sign is a minimal increase or decrease in the density of the entire bone. Most lesions of the vertebrae occur in the bodies and are of a mixed type (Fig. 2). Collapse of the body occasionally occurs, but this is less frequent than with metastatic carcinoma or lymphosarcoma. A marked deformity seldom results because the intervertebral disks are characteristically spared. When sclerotic changes occur they are usually in the vertebral bodies (Fig. 3). Involvement of the skull, ribs, and sternum is primarily of an osteolytic type (Figs. 4 and 5). In the pelvis the disease is usually found in the wings of the ilia adjacent to the sacroiliac joints. Here the process is of the mixed type giving rise to a "soap bubble" appearance (Fig. 6). Occasionally a combination of osteolytic and osteoblastic reactions with periosteal new bone formation will mimic Paget's osteitis deformans. In long bones the lesions are usually in the metaphyses and appear as rounded defects which sometimes erode the cortex (Figs. 7 and 8). Fractures do not occur often in these involved long bones (8).

DIFFERENTIAL DIAGNOSIS

Radiographic differentiation between metastatic cancer and Hodgkin's disease is difficult because of the many features that the two conditions share. Metastatic lesions tend to be more destructive and result more frequently in pathologic fractures. Sclerotic lesions originating in the prostate and breast may be indistinguishable from those of Hodgkin's disease. The



Fig. 2. A series of films showing progressive destruction of the lumbar vertebral bodies over a period of two years. Note the sparing of the intervertebral disks.

Fig. 3.

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Fig. 3. A sclerotic lesion of the twelfth thoracic vertebral body.



Fig. 4. An expanding lesion of the sternum. The sclerotic component is more marked than usual.

similarity to multiple myeloma is understandable when one considers the histologic relationship of plasmacytoma, reticulum-cell sarcoma, and Hodgkin's disease. In Hodgkin's disease the borders of the punched-out areas tend to be less distinct. Other lymphomas may require hemograms for differentiation. Osteomyelitis may be distinguished by the shaggy periosteal reaction and sequestration. Tuberculosis may present a difficult differential problem. The intervertebral disks are usually involved in tuberculosis, and gibbus deformity is common. The pain of tuberculosis responds to immobilization, while that of Hodgkin's disease responds to radiotherapy.

THERAPY

The aim of any form of therapy in Hodgkin's disease in bone is palliation. The symptoms are in themselves adequate indication for treatment, since lesions may be present for many months before they



Fig. 5. A pure osteolytic lesion of the skull.

become manifest radiographically. The most effective and best localized form of treatment is roentgen irradiation. The radiomimetic alkylating agents produce similar responses but to a lesser degree. The granulomatous tissue of Hodgkin's



Fig. 6. Typical "soap bubble" appearance of a lesion in the ilium.

disease in bone is almost as radiosensitive as in other tissues. Osteolytic lesions respond most readily. Relief is usually prompt even when the disease process is extensive. Treatment in Evanston Hospital was performed with orthovoltage equipment (210 kvp with h.v.l. 1.5 mm. Cu, or 250 kvp with h.v.l. 2.75 mm. Cu). A central axis depth dose in the order of 1,500 r in ten days was found to be adequate for relief of symptoms and arrest of the process. This corresponds to the published irradiation schedules of other authors (12, 15). Restoration of normal bone architecture may occur in the smaller lesions. The larger lesions heal by fibrosis. If the treatment is inadequate, nests of reticuloendothelial cells remain, from which the tumor may regrow (12). Occasionally after treatment an excess of new bone formation results in an ivory bone (11).

SUMMARY

Bone lesions are found in approximately 15 per cent of all cases of Hodgkin's disease antemortem. They may occur in any

phase of the disease and do not affect the other signs, symptoms, or the prognosis. The histologic findings are the same as in non-osseous lesions. Pain with or without a mass is the most frequent symptom.



Fig. 7. Lesions of the acetabulum and femoral head and neck.

Substantially all patients with Hodgkin's disease have involvement of the bone marrow. This must be distinguished from cortical lesions, which are more often apparent and symptomatic.

Approximately two-thirds of the lesions seen on radiographs show mixed osteoblastic and osteolytic reactions. Most of the remainder are destructive. In rare instances the lesions may be sclerotic.

The bone lesions are relatively radiosensitive and respond well to moderate doses of radiation. X-ray therapy is superior for the treatment of localized lesions. Alkylating agents are of use in widespread disease.

ACKNOWLEDGMENT: We are pleased to acknowledge the kindness of Dr. William T. Moss, who made

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Fig. 8. Two films demonstrating progress of a markedly destructive lesion in one year.

available the records of the Veterans Administration Research Hospital, Chicago, Ill.

Evanston Hospital Association
2650 Ridge Ave.
Evanston, Ill.

REFERENCES

1. ACKERMAN, L. V., AND DEL REGATO, J. A.: Cancer: Diagnosis, Treatment, and Prognosis. St. Louis, C. V. Mosby Co., 2d ed., 1954.
2. ASKANAZY, M.: Zentralbl. f. allg. Path. u. path. Anat. **31**: 557, 1920.
3. CRAVER, L. F., AND COPELAND, M. M.: Changes in Bone in Hodgkin's Granuloma. Arch. Surg. **28**: 1062-1086, June 1934.
4. DRESSER, R., AND SPENCER, J.: Hodgkin's Disease and Allied Conditions of Bone. Am. J. Roentgenol. **36**: 809-815, December 1936.
5. EWING, J.: Neoplastic Disease. Philadelphia, W. B. Saunders Co., 4th ed., 1940.
6. GROSSMAN, WEIS, AND OSTBORN: Fortschr. a. d. Geb. d. Röntgenstrahlen **29**: 509, 1922.
7. HANDLEY, W. S.: Cancer of the Breast and Its Treatment. New York, Paul B. Hoeber, 1922.
8. JACKSON, H., JR., AND PARKER, F., JR.: Hodgkin's Disease; Involvement of Certain Organs. New England J. Med. **232**: 547-559, May 17, 1945.
9. KOLODNY, A.: Relation of Bone Marrow to Lymphatic System; Its Role in Spreading of Carcinomatous Metastases Throughout Skeleton. Arch. Surg. **11**: 690-707, November 1925.
10. MOIR, P. J., AND BROCKIS, J. G.: Observations on Bone Lesions in Hodgkin's Disease. Brit. J. Surg. **36**: 414-417, April 1949.
11. SCHINZ, H. R., BAENSCH, W. E., FRIEDL, E., AND UEHLINGER, E.: Roentgen-Diagnostics. First American Edition (based on the fifth German edition) edited by J. T. Case. New York, Grune & Stratton, Inc., 1951, Vol. I, p. 609.
12. SLAUGHTER, D. P., AND CRAVER, L. F.: Hodgkin's Disease: Five Year Survival Rate; Value of Early Surgical Treatment; Notes on Four Cases of Long Duration. Am. J. Roentgenol. **47**: 596-606, April 1942.
13. STEINER, P. E.: Hodgkin's Disease: Incidence, Distribution, Nature and Possible Significance of Lymphogranulomatous Lesions in Bone Marrow; Review with Original Data. Arch. Path. **30**: 627-637, December 1943.
14. UEHLINGER, E.: Über Knochen-Lymphogranulomatose. Virchows Arch. f. path. Anat. **288**: 36-118, 1933.
15. VIETA, J. O., FRIEDEL, H. L., AND CRAVER, L. F.: A Survey of Hodgkin's Disease and Lymphosarcoma in Bone. Radiology **39**: 1-14, July 1942.
16. WILLIS, R. A.: The Spread of Tumours in the Human Body. London, Butterworth & Co., Ltd., 1952.
17. WOODARD, H. Q., AND CRAVER, L. F.: Serum Phosphatase in Lymphomatoid Diseases. J. Clin. Invest. **19**: 1-7, January 1940.

SUMMARIO IN INTERLINGUA

Morbo de Hodgkin in Osso

Super le base de un revista de litteratura e un studio de 94 casos de morbo de Hodgkin, incluse 11 que monstrava affectiones ossee, le autores del presente communication ha arrivato al sequente conclusiones:

Lesiones ossee es trovate ante morte in approximativemente 15 pro cento de omne casos de morbo de Hodgkin. Illos pote occurrer in non importa qual phase del morbo e non affice le altere signos e symptomatas o le prognose. Le constatationes histologic es le mesmes como in lesiones non-ossee. Dolor con o sin le presentia de un massa es le symptoma le plus frequente.

Plus o minus omne le patientes con

morbo de Hodgkin monstra un affection del medulla ossee. Isto debe esser distinguite ab lesiones cortical que es plus frequentemente apparente e symptomatic.

Approximativemente duo tertios del lesiones vidite in radiographias monstra mixte reactiones osteoblastic e osteolytic. Le majoritate del remanentes es destructive. In rar casos, le lesiones pote esser sclerotic.

Le lesiones ossee es relativemente radiosensibile e responde ben a moderate doses de radiation. Roentgenotherapie es superior in le tractamento de lesiones localisate. Agentes alcoylante es de uso in casos de extense morbiditate.



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Paraffin Base Halogenated Hydrocarbon Chemical Dosimeters¹

MAJIC S. POTSAID, M.D.,² and GORO IRIE, M.D.³

A SENSITIVE colorimetric measure of radiation absorbed dose (rad) has long been needed, and many studies have been directed toward finding a usable system. The value of a phantom for this purpose would be further increased if the material density were closely equivalent to tissue, with degrees of absorbed dose delineated by different colors within the phantom itself. With the use of halogenated hydrocarbons in a paraffin base a practical in-phantom ionizing radiation colorimetric dosimeter has been devised and successfully applied to dose distribution.

Halogenated hydrocarbons were among the first groups of chemicals tried for radiation dose determinations. As early as 1904 iodoform dissolved in chloroform was reported as demonstrating radiation effects, but the mixture was relatively unstable (1). In 1928 the liberation of chlorine from chloroform to form an acid was considered to be proportional to radiation energy absorbed (2). Later investigations revealed that halogenated hydrocarbons exhibited many properties essential to a practical dosimeter (3). Because long chain chemical reactions can occur during irradiation of halogenated hydrocarbons, especially in the presence of small amounts of oxygen, the G value (number of acid molecules formed per 100 ev) of these compounds has been estimated to be extremely high under some conditions (4).

Halogenated hydrocarbon radiation dosimeters have been studied particularly as liquid aqueous and non-aqueous systems (5). This report concerns the usefulness of bromoform and chloroform in solid non-aqueous chemical dosimeters that clearly give a three-dimensional isodose picture of



Fig. 1. Aluminum mold for making 20 × 20 × 2-cm. slabs of dosimeter.

absorbed dose from all forms of ionizing radiation.

MATERIALS AND METHODS

Solid paraffin and paraffin-wax combinations were mixed with chloroform and bromoform in concentrations of halogenated hydrocarbon ranging from 4 to 40 per cent by weight. Each kilogram of mixture contained 100 mg. of methyl yellow [*p*-dimethyl aminoazobenzene, $(\text{CH}_3)_2\text{NC}_6\text{H}_4\text{N}:\text{NC}_6\text{H}_5$]. The azo dye was dissolved in chloroform or bromoform and added carefully to melted paraffin or paraffin-wax, which was usually kept between 70 and 80°C. Such mixing produced no significant loss of halogenated hydrocarbon by evaporation.

Various plant and animal waxes in amounts ranging from 0 to 50 per cent were added to purified solid paraffins of different molecular weights and physical properties (hardness and melting point). Blending temperatures were kept slightly above the melting points of the materials.

The melted phantom material was then poured into and allowed to solidify in an aluminum mold (Fig. 1) which had been siliconed previously by baking on a thin

¹ From Harvard Medical School and Massachusetts General Hospital, Boston, Mass. Accepted for publication in December 1960.

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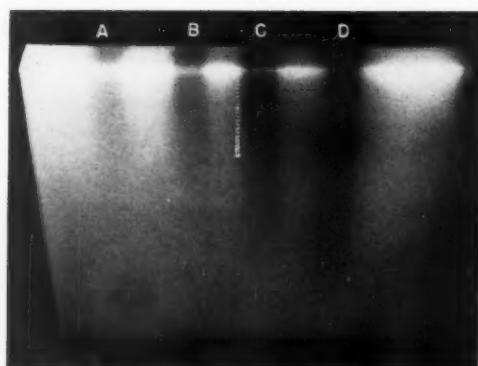


Fig. 2. Intensification of color with increased dose of x-rays (280 kvp, 1.3 mm. Cu h.v.l.). A. 500 r. B. 1,000 r. C. 2,000 r. D. 4,000 r.

layer of SC-87 Dri-Film.⁴ Silicone treatment of the mold was necessary to facilitate separation of dosimeter material from metal.

The light yellow slabs or blocks arranged in the desired geometry of phantom have been irradiated by 200 kvp (0.65 mm. Cu h.v.l.), 280 kvp (1.3 mm. Cu h.v.l.), and 2,000 kvp (13 mm. Cu h.v.l.) x-rays, with various field sizes, collimators, and grids. Gamma-ray isodose patterns have been determined for a Co⁶⁰ teletherapy unit and radium applicators employed in radiation therapy. To study corpuscular radiation effects a Sr⁹⁰-Y⁹⁰ plaque provided a satisfactory source of electrons.

RESULTS

Ionizing radiation instantly caused the irradiated portion of the yellow phantom to become red with an intensity of color proportional to the amount of absorbed dose (Fig. 2). In mixtures containing higher concentrations of bromoform, a faint red conversion was noticeable by gross inspection at doses less than 100 rads. However, the bromoform dosimeter was also sensitive to ordinary light at the higher energy end of the spectrum and found to be less practical than the chloroform system, which had to be protected only from prolonged direct daylight. Since

⁴General Electric Co., Silicone Products Dept., Waterford, N. Y.

30 per cent chloroform-paraffin-wax mixtures have a specific gravity around 1.0, such concentrations were used when material more closely equivalent to tissue was desired. For the usual applications, however, a 7 to 8 per cent chloroform concentration was considered most useful.

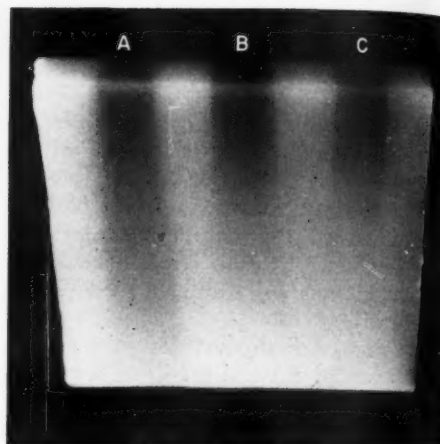


Fig. 3. Increase in depth dose with higher quality x-rays, 2,000 r at surface of each field. A. 2,000 kvp, 13 mm. Cu h.v.l. B. 280 kvp, 1.3 mm. Cu h.v.l. C. 200 kvp, 0.65 mm. Cu h.v.l.

It was found that hard paraffins with a melting point between 65 and 70°C. were most practical from the standpoint of firmness of phantom when mixed with chloroform. Upon solidification, however, most paraffins without wax resulted in excessive flaking and internal cracking, which disrupted visual uniformity of the isodose patterns. Purified beeswax (Myricyl palmitate, $C_{15}H_{31}COOC_{31}H_{63}$) in small amounts (0.2 to 1 per cent) was especially effective in eliminating flaking and cracking and did not significantly lower radiation sensitivity of the dosimeter. When greater percentages of beeswax were used, as much as 2,000 rads were needed to produced a moderate red color.

Demonstrations of increased depth dose with higher quality x-rays or larger field size (Fig. 3), as well as depth distribution of radiation passing through grids (Fig. 4), have been easily achieved. Recorded by the dosimeter were effects of multiple fields and rotation technics on relative

dose in various parts of a particular geometry (Fig. 5).

No difficulty has been encountered in delineating isodose patterns around radium sources (Fig. 6) or picturing the absorbed dose beneath a beta source radioactive plaque.

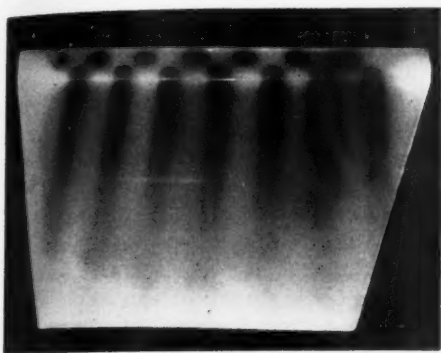


Fig. 4. Dose distribution resulting from interposition of a 40 per cent Hirsch Marks therapy grid between x-ray source (280 kvp, 1.3 mm. Cu h.v.l.) and phantom.

During one of the first trials of the dosimeter, unsharp edges were produced in a field of radiation by a beam of x-rays from a well collimated unit with a newly installed tube. A fuzzy penumbra, wider than anticipated, had resulted. A careful check of the machine revealed that the focal spot area was four times larger than it should have been, due to an improper resistor that did not optimally focus the electron beam on the target. In another instance, a further trial of the dosimeter clearly demonstrated that the actual radiation field and the field delineated by the light localizer were not the same because of a misalignment of mirrors. These defects were discovered during sensitivity trials of different dosimeter mixtures and had not been looked for specifically.

DISCUSSION

Present studies indicate that a paraffin-chloroform chemical dosimeter has value as affording an immediate record of relative quantity of absorbed dose in different parts of a solid phantom of particular geometric arrangement. One exposure gives

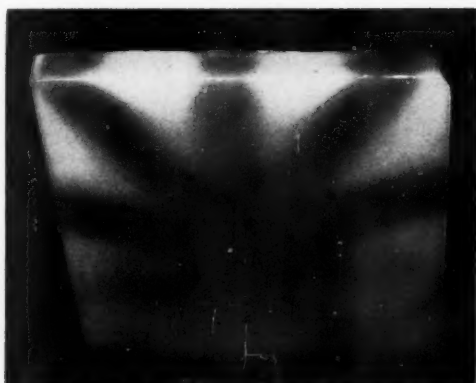


Fig. 5. Build-up of depth dose at the central axis of a multiple field geometry with 1,000 r delivered at the surface of each port from a Co^{60} teletherapy unit.

a complete three-dimensional picture of dose with no concern as to the accurate maintenance of geometry such as is necessary in multiple measurement techniques for obtaining isodose curves. To date the system appears to be more reproducible and constant than chloroform aqueous systems which require considerable purity control. There was little or no energy or dose rate dependence evident within certain moderate ranges (50–2,000 kvp, 1 to 1,000 rad per minute). Higher energies and dose rates are to be examined.

Like other halogenated hydrocarbon systems, these dosimeters also are sensitive to quanta of energy lower than ionizing radiation and must be protected especially from ultraviolet light and direct daylight. To keep an irradiated phantom for weeks with its pattern of dose intact often necessitates wrapping it in dark paper during storage in a cool place. Keeping a radiation-exposed dosimeter in a refrigerator also reduces diffusion of the halogenated hydrocarbon, lessens distortion of the pattern, and protects against fading of color. Preliminary trials of other halogenated hydrocarbons and other indicators show promise of application in the solid paraffin system.

Pilot studies suggest that small amounts of oxygen are essential in the paraffin system to maintain the apparently high G value of some mixtures. In other ex-

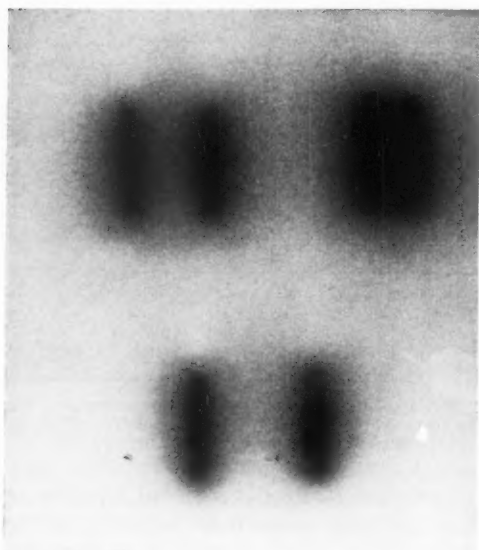


Fig. 6. Dose distribution around pairs of 50-mg. radium slugs 3 cm. in length, with 1, 2, and 3 cm. separation of sources. Six-hour exposure.

periments in which liquid paraffins were substituted for solid substances, a decrease in sensitivity to radiation was observed. This apparent shortening of the chain reaction may indicate less radiation response in some liquid systems because of increased mobility of the molecules, the effect of smaller molecules, or both.

Water in the dosimeter markedly decreases the radiation response. Even the small amount of water that may find its way into the system as a consequence of washing the halogenated hydrocarbon or liquid paraffin can produce this effect. Other types of compounds, particularly synthetic rubbers, can reduce the internal cracking and flaking of paraffin and may prove to be more desirable than waxes.

The phantom dosimeter with a paraffin base can be easily sectioned to determine more precisely the three-dimensional dose distribution, but it has other disadvantages as has been pointed out. A search is under way to find bases that may be transparent, firmer in structure, as well as tissue-equivalent. Perhaps colorimetric changes can be produced in some plastic materials at reasonable levels of radiation, and

polymerization technics may be devised to form a hard transparent phantom.

Some commercially available paraffins used for the mounting and sectioning of tissues have physical and chemical properties similar to the paraffin-wax base described above and have been found conveniently applicable. "Tissuemat," with a favorable 61°C. melting point, has been found suitable and has been used for most of the illustrations of the dosimeter. It must be kept in mind that some tissue-mounting materials may contain antioxidants that can adversely affect sensitivity to radiation.

It is expected that solid phantom radiation dosimeters will have many applications, not only for research and teaching but also for routine problems in radiology. Some uncertain isodose patterns will be clarified and unexpected distributions of absorbed dose will be uncovered. In addition to the previously mentioned uses of the phantom dosimeter the following radiation problems offer intriguing avenues of future approach:

Determination by electron magnetic resonance of the degree of trapped free radical formation and its relation to color change.

Study of oxygen and anoxia effects in a solid system.

Exploration of the interesting change in sensitivity of the paraffin dosimeter induced by small amounts of water.

Determination of absorbed dose adjacent to bone as a function of radiation quality (h.v.l.).

Demonstration of isodose patterns produced by neutron sources and beams.

Visualization of the Bragg peak as produced by protons and other ions.

Demonstration of the effect of uneven surfaces on isodose curves and depth dose.

Development of a quantitative spectrophotometric method to measure absolute dose by transmittance, absorbance, or reflectance, using the color changes in a paraffin dosimeter.

* Fisher Scientific Co., 1 Reagent Lane, Fair Lawn, N. J.

CONCLUSION

An easily constructed and conveniently applied solid phantom chemical dosimeter can be made from chloroform, paraffin, beeswax, and methyl yellow. It gives a clear three-dimensional isodose picture of absorbed dose from all forms of ionizing radiation.

REFERENCES

1. FREUND, L.: Wien. klin. Wchnschr. **17**: 417, 1904.

2. GÜNTHER, P., VON DER HORST, H. D., AND CRONHEIM, C. F.: Ztschr. Electrochem. **34**: 616, 1928.

3. CLARK, G. L.: Applied X-rays. New York, McGraw-Hill Book Co., Inc., 4th Ed., 1955. Chapter 11: The Chemical Effects of X-rays.

4. HINE, G. J., AND BROWNELL, G. L., editors: Radiation Dosimetry. New York, Academic Press, Inc., 1956. Chapter 8: Chemical and Colorimetric Indicators, by G. V. Taplin.

5. CLARK, G. L., AND BIERSTEDT, P. E., JR.: X-Ray Dosimetry by Radiolysis of Some Organic Solutions. 1. Dithizone and Methyl Yellow Solutions. Radiation Res. **2**: 199-218, May 1955.

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SUMMARIO IN INTERLINGUA

Dosimetros Chimic de Halogenate Hydrocarburo a Base de Paraffin

Un sensibilissime mesura colorimetric del dose de radiation absorbite (= rad) es de post longe tempores un desiderato urgente, e multe studios ha essite dedicate al discoperta de un usabile systema. Le autores del presente communication ha trovate que un dosimetro chimic facite de chloroformo, paraffin, cera de ape, e jalne methylic rende possibile le obtention de un

registracion immediate del quantitate relative de dose absorbite in diverse partes de un phantoma solide. Un exposition provide un complete pictura tri-dimensional del dose absorbite ab omne formas de radiation ionisante.

Applicationes possibile de un tal dosimetro de radiation a phantoma solide es discutite.



Co⁶⁰ Isodose Curves for 240° Rotation, Showing Displacement of the Center of Dose from the Center of Rotation¹

LILLIAN E. JACOBSON, M.A., GEORGE P. KOECK, M.D., WILLIAM R. HILLSINGER, B.S.,
and MARK E. SCHWARZ, B.A.

THIS INVESTIGATION was undertaken in order to find the dosage distribution within the tumor and surrounding tissues when a patient is treated by a partial rotation technic with a Co⁶⁰ teletherapy machine. The published isodose curves and data (1-6) were not sufficiently extensive for our purposes, especially when the rotation was limited to an arc of 240°, the maximum traversed by the Picker C-3000 machine. Partial rotation is valuable in many problems of therapy; for example, treatment around the bladder, uterus, and rectum. Hence, it may be used on

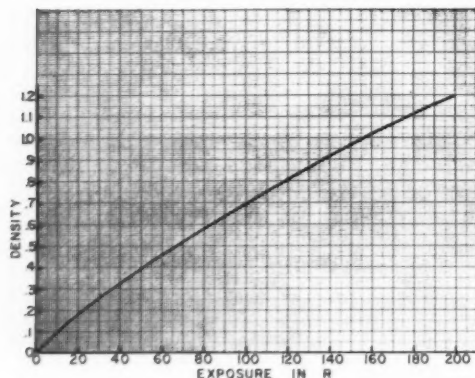


Fig. 1. Calibration curve of density vs. exposure in roentgens.

machines with which full rotation is possible. This study, therefore, includes 240° rotation for the 360° rotation Picker C-1000 machine.

METHOD

A sheet of du Pont Adlux film was placed between two elliptical sections—each 1 cm. thick—of a unit-density Masonite Presdwood phantom. The assembly was

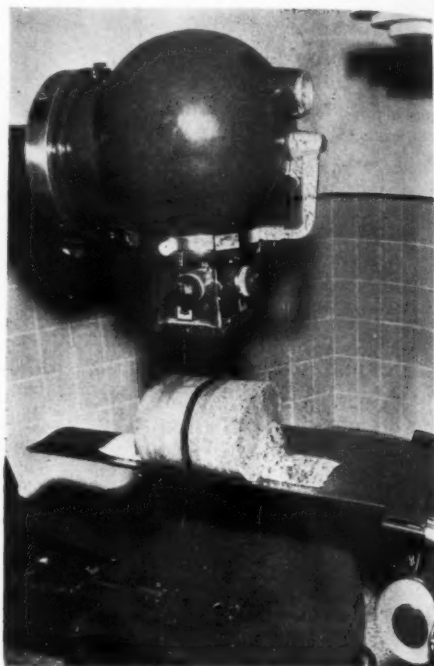


Fig. 2. Set-up of phantom with cobalt machine.

made light-tight by pasting black Scotch electrical tape over the edge of the boards. Films were exposed to 10 r, 25 r, 50 r, 100 r, 150 r, and 200 r. These, together with an unexposed film, were pan developed, fixed, and washed. The maximum density at the center of the exposed film was measured on a Photovolt transmission densitometer set for zero reading for the unexposed film density. Seven sets of films were exposed, developed, and measured similarly. Density-dosage curves were plotted. All seven curves had essentially the same shape but differed in slope due to variable temperature and

¹ From the Radiation Therapy Department of The Presbyterian Hospital Unit of the United Hospitals of Newark, Newark, N. J. Presented at the Forty-sixth Annual Meeting of the Radiological Society of North America, Cincinnati, Ohio, Dec. 4-9, 1960.

time conditions of developing. At the point of greatest spread, the 200 r exposure, the greatest variation in density was 8 per cent. An average curve was plotted from these seven curves. This became the density-dose calibration curve (Fig. 1).

Each section of the Presdwood phantom had a long axis of 29.5 cm. and a short axis of 23 cm. The boards containing the film were placed in the middle of the phantom

an unexposed portion of the same film, was developed and measured on the densitometer. The density was read at centimeter intervals along axes from the center of rotation, spaced 30° apart. By the use of the density-dose calibration curve the roentgen values were found. From these the per cent of maximum dose at all the measured points was calculated. Each family of curves involved about 750 determinations.

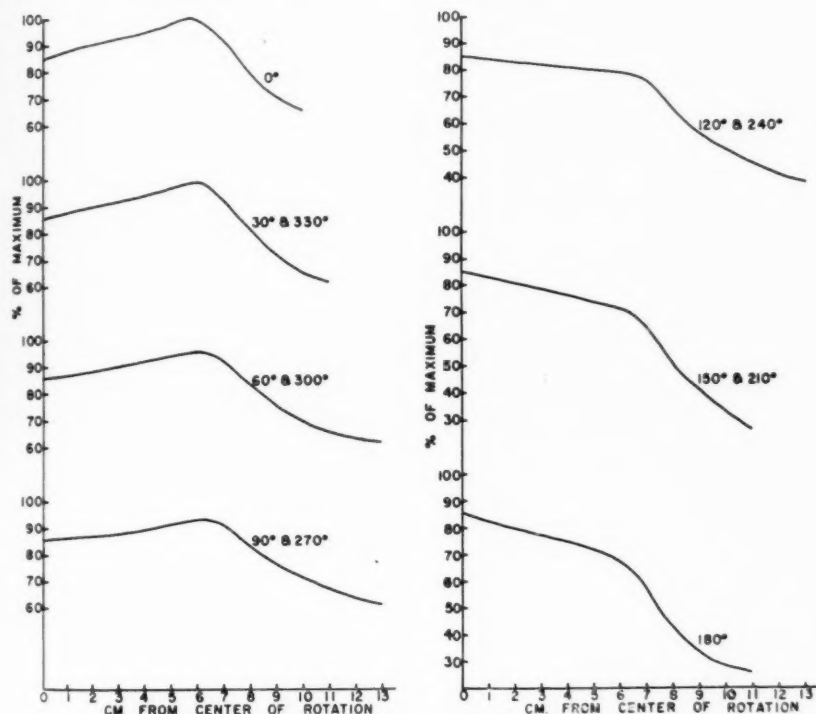


Fig. 3. Family of average curves of per cent of maximum dose vs. distance from the center of rotation for the C-3000 and a 14 × 15-cm. field at 95 cm. S.A.D., 240° rotation.

with 11.5 cm. thickness of Presdwood on either side of the film. The boards making up the phantom were held together by small plastic pegs at the edge of the sections and sand bags at both ends. The phantom was placed on the table, lined up so that the plane of the film was in the plane of rotation and the center of rotation at the center of the phantom section containing the film. The set-up is shown in Figure 2. The exposed film, together with

Curves of per cent of maximum dose versus distance from the center of rotation for the different axes were plotted. Three separate films for each field size were exposed and worked up. The exposures were on different dates, so that the conditions of development for each film were slightly different. Yet the curves agreed closely with one another. An average family of curves was plotted for the dose distribution along each axis (see Fig. 3).

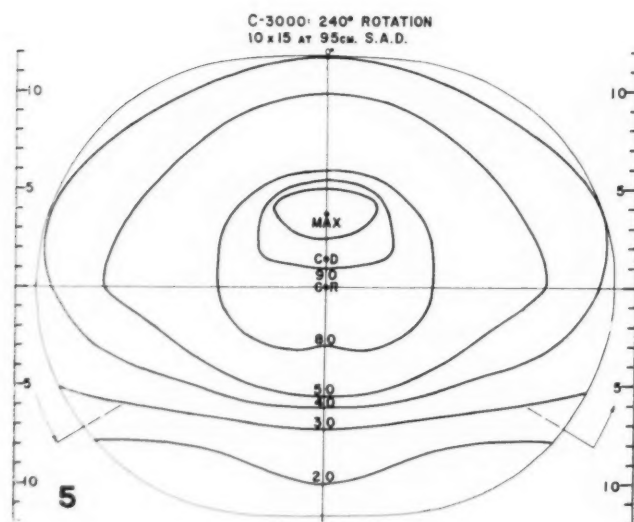
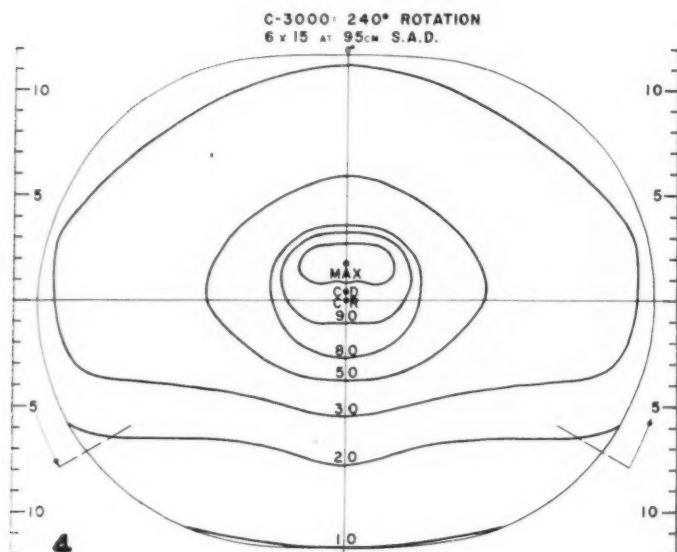


Fig. 4. C-3000 isodose curves for a 6 × 15-cm. field at 95 cm. S.A.D., 240° rotation.

Fig. 5. C-3000 isodose curves for a 10 × 15-cm. field at 95 cm. S.A.D., 240° rotation.

By the use of these, isodose curves were calculated and plotted for each field size.

RESULTS

In the Picker C-3000 cobalt teletherapy machine the source is 2 cm. in diameter and is 95 cm. from the axis of rotation. Iso-

dose curves were made for 240° rotation for fields of the following dimensions: 6 × 15 cm. (Fig. 4), 10 × 15 cm. (Fig. 5), 14 × 15 cm. (Fig. 6), 17 × 15 cm. (Fig. 7).

The Picker C-1000 cobalt teletherapy machine has a special source 1 cm. in diameter. The source-axis distance

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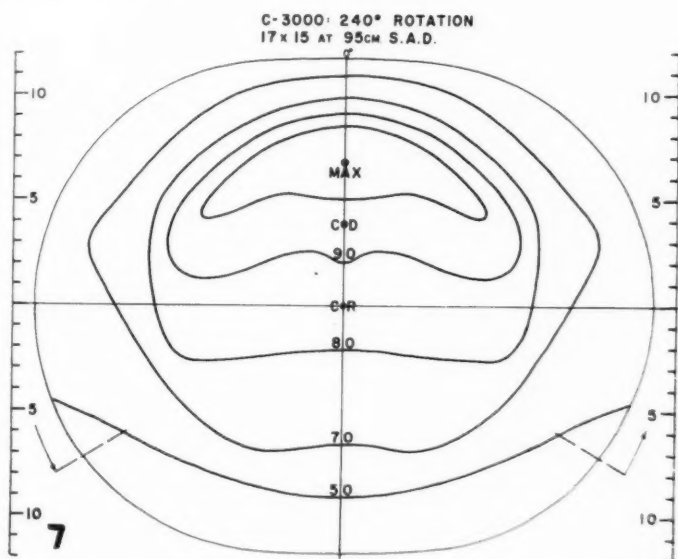
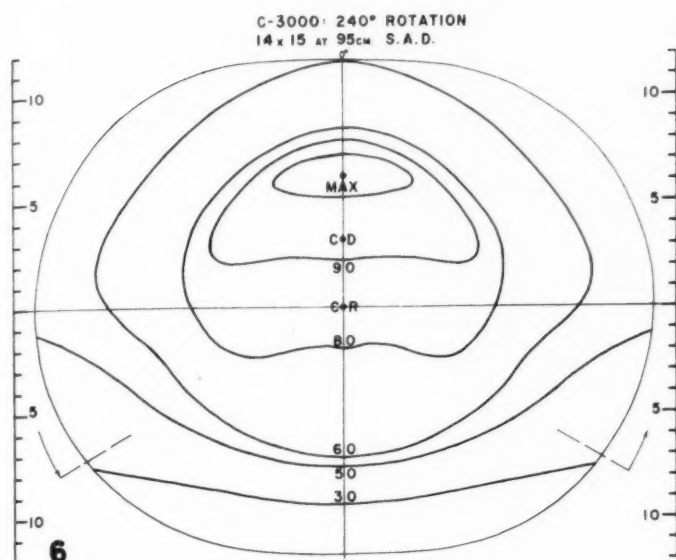


Fig. 6. C-3000 isodose curves for a 14 × 15-cm. field at 95 cm. S.A.D., 240° rotation.

Fig. 7. C-3000 isodose curves for a 17 × 15-cm. field at 95 cm. S.A.D., 240° rotation.

(S.A.D.) is 55 cm. Isodose curves were made for 240° rotation for fields 6 × 15 cm. (Fig. 8), 10 × 15 cm. (Fig. 9), 14 × 15 cm. (Fig. 10), 17 × 15 cm. (Fig. 11).

Films were exposed and measured and the results were plotted for field sizes of 6 × 6 cm. and 10 × 10 cm. These were almost the same as for 6 × 15 cm. and 10 × 15

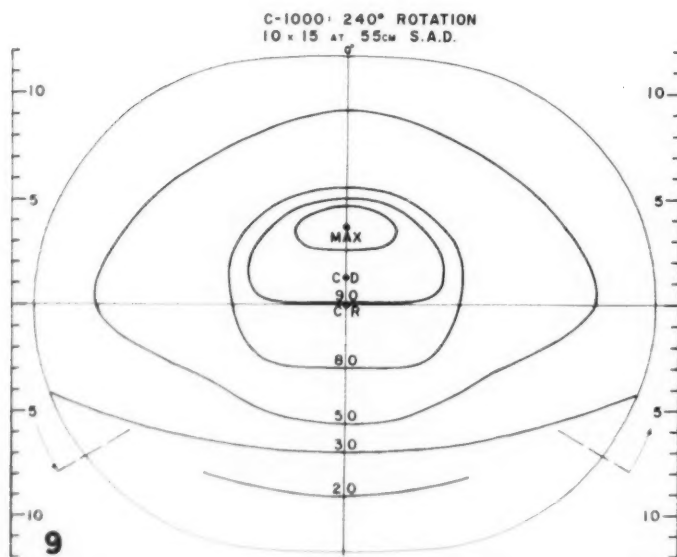
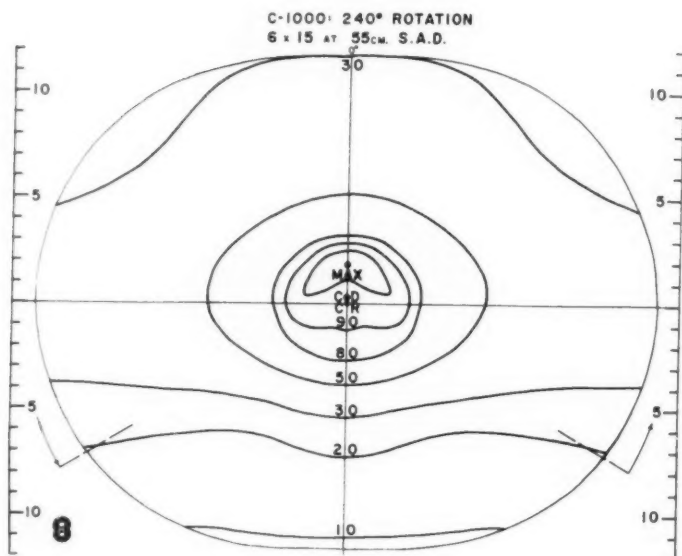


Fig. 8. C-1000 isodose curves for a 6 x 15-cm. and a 6 x 6-cm. field at 55 cm. S.A.D., 240° rotation.

Fig. 9. C-1000 isodose curves for a 10 x 15-cm. and a 10 x 10-cm. field at 55 cm. S.A.D., 240° rotation.

cm., respectively. The size of the opening in the plane of rotation and not perpendicular to it determines the shapes of the isodose curves.

If the displacement of the center of the 97 per cent isodose line, which we call the maximum isodose line, from the center of rotation is plotted *versus* the dimension

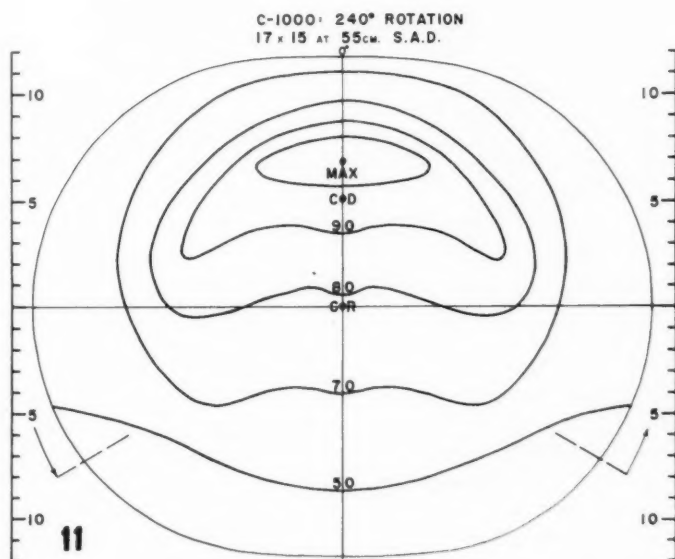
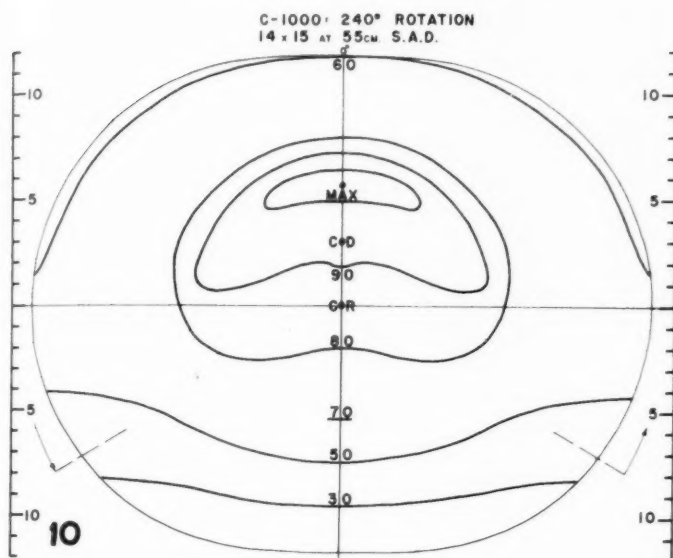


Fig. 10. C-1000 isodose curves for a 14 x 15-cm. field at 55 cm. S.A.D., 240° rotation.

Fig. 11. C-1000 isodose curves for a 17 x 15-cm. field at 55 cm. S.A.D., 240° rotation.

of the field in the plane of rotation, the width, the family of curves shown in Figure 12 is obtained. The center of dose for both cobalt machines is displaced away from the untreated sector by 1.8 cm. for

a field width of 6 cm., and approximately 7 cm. for a field width of 17 cm.

Since, with cobalt radiation, we do not have a sharp cut-off where the field ends, the 80 per cent isodose line is considered the

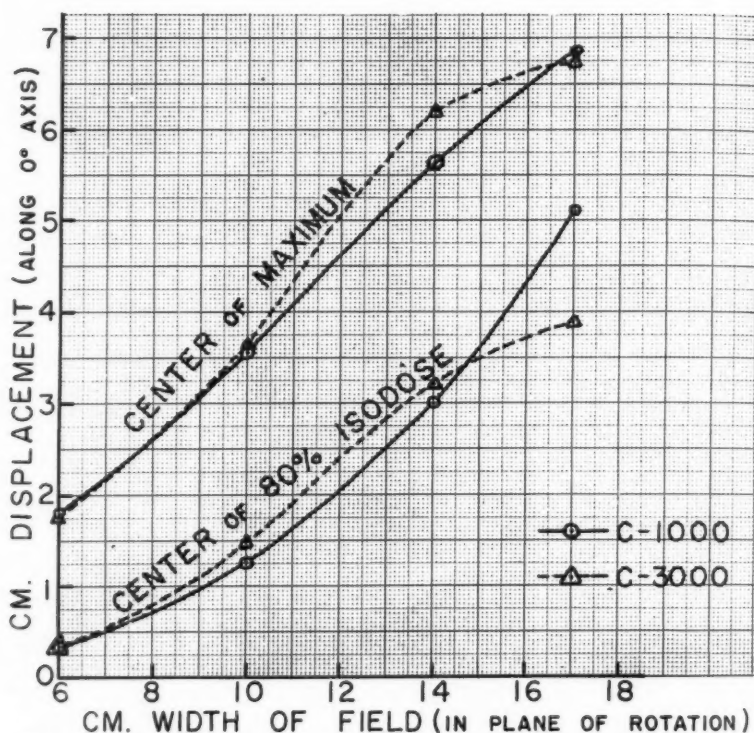


Fig. 12. Family of curves for 240° rotation showing displacement of the center of (A) maximum dose from the center of rotation for C-3000 machine at 95 cm. S.A.D. and for C-1000 machine at 55 cm. S.A.D.; (B) of 80 per cent isodose curves from the center of rotation for C-3000 machine at 95 cm. S.A.D. and for C-1000 machine at 55 cm. S.A.D.

edge of the field. The center of this isodose line is therefore the center of the field.

The displacement of the center of the 80 per cent isodose curves from the center of rotation is less than that for the center of the maximum isodose curves. For the C-3000 the displacement of the center varies from 4 mm. for a 6 cm. width of field to 4 cm. for a 17 cm. width. For the C-1000, the displacement of the center varies from 3 mm. for a 6 cm. width of field to 5 cm. for a 17 cm. width. The importance of this displacement will be discussed later.

As the dimension in the plane of rotation is increased, the center of dose is shifted further away from the untreated sector. The isodose curves become less circular, appearing like a punctured rubber ball,

one of whose sides has been squeezed in toward the other side. The displacement of the center of the 80 per cent curve is greater for the shorter S.A.D. of 55 cm. on the C-1000 machine than for the S.A.D. of 95 cm. on the C-3000 machine.

Isodose curves were made for 360° rotation on the C-1000 machine for a field of 10 × 10 cm. These are shown in Figure 13. The curves are slightly elongated along the short axis of the phantom, as one would expect. They are in fairly good agreement with curves previously published (2).

APPLICATIONS OF ISODOSE CURVES

We have found the isodose curves very useful in treatment planning. Even if the dimensions of the patient are different from those of the phantom, the per cent

isodose curves still hold. When the patient is thicker, if the assumption is made that an annular ring of uniform thickness is added to the phantom, the time to give the required number of r at the center increases, but the per cent of the central dose received at given distances from the position of maximum dose remains unchanged. Therefore, these isodose curves can be used in treatment planning for other dimensions than the thickness of our phantom.

lateral aspects of the contour and then on the patient, using the reference points previously marked on the patient. Other "critical tissues" may also be outlined within the tracing contour. The isodose curves which enclose the required field size are put under the tracing paper outline with the center of the 80 per cent isodose line at the center of the tumor (see Fig. 14). The center of rotation is marked on the tracing paper and is projected anteriorly and laterally. The distance between

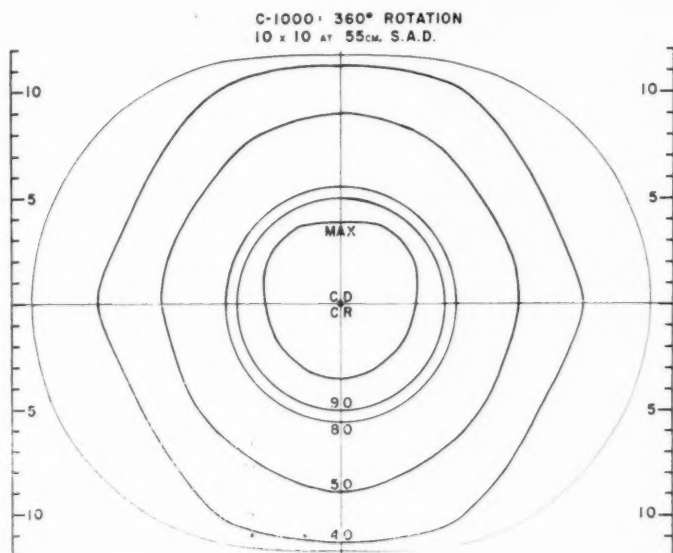


Fig. 13. C-1000 isodose curves for a 10 × 10-cm. field and 360° rotation at 55 cm. S.A.D.

We will describe our method: The contour of the patient through the central section is obtained with a strip of plaster-of-paris. Certain reference points are marked on the patient and on the contour strip. The contour is then transferred to tracing paper and the reference points are marked. Anteroposterior and lateral views are taken of the patient, with special lead markers on the reference points, and the tumor is localized on these films. After allowance has been made for magnification, the outline of the tumor is transferred to the tracing paper. The center of the tumor is projected on the anterior and

the lateral projections of the center of rotation and the center of the lesion will serve to locate the projection of the center of rotation on the lateral aspects of the patient. The depth of the center of rotation from the anterior surface of the skin can also be found. The usual method of positioning the patient for the particular machine can then be followed.

If one does not draw the contour, the displacement of the center of the 80 per cent isodose line from the center of rotation for the desired field size can be found on the curves in Figure 12. Let us suppose that the anterior and lateral projections

TABLE I: DISPLACEMENT OF THE CENTER OF THE 97 PER CENT ISODOSE LINE FROM THE CENTER OF ROTATION, FOR 240° ROTATION, FOR DIFFERENT WIDTHS OF FIELDS FOR S.A.D.'s OF 95 AND 55 CM.

Width of Field in plane of rotation (cm.)	Displacement for an S.A.D. of 95 cm. for C-3000 (cm.)	Displacement for an S.A.D. of 55 cm. for C-1000 (cm.)
6	1.8	1.8
8	2.6	2.6
10	3.7	3.6
12	5.1	4.6
14	6.2	5.6
16	6.6	6.5
17	6.8	6.7

TABLE II: DISPLACEMENT OF THE CENTER OF THE 80 PER CENT ISODOSE LINE FROM THE CENTER OF ROTATION, FOR 240° ROTATION, FOR DIFFERENT WIDTHS OF FIELDS FOR THE C-3000 AT 95 CM. S.A.D. AND THE C-1000 AT 55 CM. S.A.D.

Width of Field in Plane of Rotation (cm.)	Displacement for an S.A.D. of 95 cm. for C-3000 (cm.)	Displacement for an S.A.D. of 55 cm. for C-1000 (cm.)
6	0.4	0.3
8	0.8	0.7
10	1.5	1.3
12	2.4	2.0
14	3.2	3.0
16	3.7	4.3
17	3.9	5.1

of the center of the tumor have been marked on the patient's skin and the size of the port at the tumor is 14 × 15 cm. The patient is being treated with a C-3000 machine and 240° rotation. The center of the 80 per cent isodose line is 3.2 cm. above the center of rotation (see Table II). Since we desire the center of the tumor at the center of the 80 per cent isodose line, the lateral projection of the center of rotation will have to be lowered 3.2 cm. from the projection of the center of the tumor on the lateral aspects of the patient. This is most important. If it is not done, parts of the tumor in the untreated 120° sector will not be given a sufficient dose and structures superior to and outside of the tumor will be overdosed, as shown in Figure 15. The center of the tumor receives about 85 per cent; the lower portion, 70 per cent; and the overlying tissue superior to and outside of the tumor, the maximum dose of 97 to 100 per cent.

The data from the curves in Figure 12 have been tabulated in Tables I and II.

If the maximum dose in the tumor is to be 100 r or 100 per cent, then the calculated dose at the center of rotation can be obtained from Table III, where the dose at the center of rotation as per cent of maximum dose is given for different widths of the field in the plane of rotation. For 14 cm. lateral width, 85 per cent of the maximum is received at the center of rotation. The time to give 85 instead of 100 r should be calculated, for when the center of rotation, for which dosage is generally calculated, receives 85 r, the tumor will receive 100 r.

The isodose curves which we use in dosage planning have been plotted to scale on developed blank du Pont Adlux films. These films are flexible and translucent. Other types of film, such as Translite, could be used. To make a set of isodose curves to scale from the isodose curves

TABLE III: DOSE AT THE CENTER OF ROTATION IN PER CENT OF MAXIMUM DOSE FOR DIFFERENT WIDTHS OF FIELDS, FOR 240° ROTATION, FOR C-3000 AT 95 CM. S.A.D. AND C-1000 AT 55 CM. S.A.D.

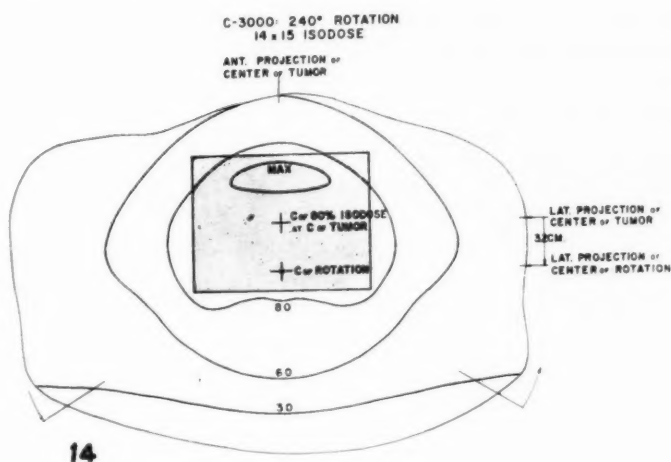
Width of Field in Plane of Rotation (cm.)	Per Cent of Maximum for S.A.D. of 95 cm. for C-3000	Per Cent of Maximum for S.A.D. of 55 cm. for C-1000
6	93	93
8	91	91
10	88	89
12	86.5	87
14	85	85
16	84.5	82
17	84	78

which are published in this paper, one should proceed as follows: Project each figure so that the scale on the side of the figure is magnified to the correct length on a sheet of tracing paper. Then trace the isodose curves. These will be to scale. These curves can be used directly or transferred to developed blank films.

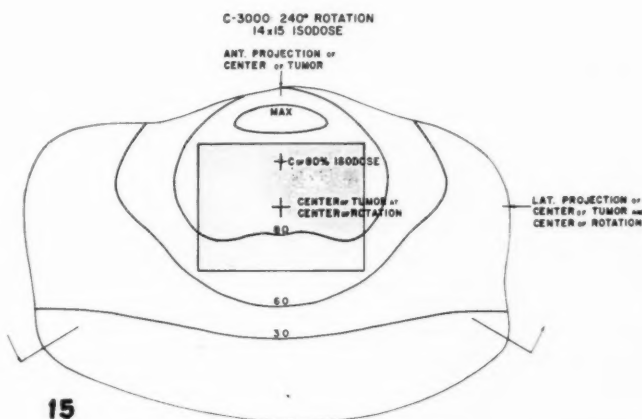
SUMMARY

1. A method of obtaining isodose curves for rotation therapy with Co⁶⁰ teletherapy machines by the use of films exposed in a Presdwood phantom and measured on a densitometer has been described.

2. Isodose curves were made for 240°



14



15

Fig. 14. Isodose curves on body contour and tumor.

Fig. 15. Isodose curves on body contour and tumor if no correction is made for the displacement of the center of dose from the center of rotation.

rotation for a Picker C-3000 and a Picker C-1000 machine for fields varying from 6 × 6 cm. to 17 × 15 cm.

3. Curves are given showing the displacement of the center of maximum dose from the center of rotation and the displacement of the center of the 80 per cent isodose curves from the center of rotation, for fields of different sizes with the C-3000 and C-1000 machines. The displacement varies from 1.8 to 7 cm. for the C-1000 with a 55 cm. source-axis distance (S.A.D.), and for the C-3000 with a 95 cm. S.A.D. The displacement for the center of the 80 per cent curves varies from 0.4 to 5

cm. for 55 cm. S.A.D., and to 4 cm. for the 95 cm. S.A.D.

4. The displacement of the center of dose depends chiefly on the dimension of the field in the plane of rotation and is almost independent of the dimension perpendicular to the plane of rotation.

5. Isodose curves for the C-1000 machine and a diaphragm setting of 10 × 10 cm. are given for 360° rotation.

6. The method of using the isodose curves for patient work is described.

7. A table is given of the dose at the center of rotation in per cent of the maximum dose for fields of different sizes.

The calculation of dose to the tumor is based on that received by the center of rotation.

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REFERENCES

1. TRUMP, J. G., WRIGHT, K. A., EVANS, W. W., HARE, H. F., AND LIPPINCOTT, S. W., JR.: Two Million

Volt Roentgen Therapy Using Rotation. *Am. J. Roentgenol.* **66**: 613-623, October 1951.

2. LANZL, L. H., AND SKAGGS, L. S.: Revolving Beam Isodose Distributions from a Cobalt-60 Therapy Unit. Argonne Cancer Research Hospital Semi-Annual Report to the U. S. Atomic Energy Commission ACRH-10, September 1958, pp. 54-72.

3. JOHNS, H. E., WHITMORE, G. F., WATSON, T. A., AND UMBERG, F. H.: A System of Dosimetry for Rotation Therapy with Typical Rotation Distributions. *J. Canad. A. Radiologists* **4**: 1-4, March 1953.

4. JONES, D. E. A., GREGORY, C., AND BIRCHALL, I.: Dosage Distribution in Rotational Cobalt 60 Therapy. *Brit. J. Radiol.* **29**: 196-201, April 1956.

5. GREGORY, C.: Dosage Distribution in Rotational Cobalt 60 Therapy. A Simplified Method of Computation. *Brit. J. Radiol.* **30**: 538-543, October 1957.

6. BURLIN, T. E.: The Evaluation of the Dose to the Thorax in Rotational Cobalt 60 Therapy. *Brit. J. Radiol.* **30**: 543-549, October 1957.

DISCUSSION

Leon Pape (Duarte, Calif.): If one does a study of the shift of peak ionization from the center of rotation as a function of the arc rotation, one finds (as might be expected) that the point of peak ionization moves from essentially the entrance surface at zero degrees rotation to a point coincident with the center of rotation at 360 degrees. The interesting thing is that one can show by geometric

consideration of the beam that, for an arc of 180 degrees, the point of peak ionization is displaced from the center of rotation by a distance equal to one-half the beam width at that point. This is a very good reference point from which to conclude the relative displacement of the point of peak ionization from the center of rotation for arcs which are greater or less than 180 degrees.

SUMMARY IN INTERLINGUA

Curvas de Isodosage de Cobalt-60 pro un Rotation de 240°, Monstrante Displaciamento del Centro del Dose ab le Centro del Rotation

Certe machinas de teletherapia a cobalt-60 pote esser rotate solmente intra 240°. Pro trovar le displaciamento del centro del dose ab le centro de rotation, curvas de isodosage pro campos de varie dimensiones esseva construite ab lecturas densitometric de pelliculas exponite intra un phantoma de Presdwood a un distantia fonte-axe de 55 e

de 95 cm. Le displaciamento varia ab 1,7 cm pro un campo de 6 × 6 cm ad 7 cm pro un campo de 17 × 15 cm. In placiari un patiente, il es necessari (1) absorber iste differentia per displaciari le centro de rotation ab le centro del tumor e (2) corrigere le tempore de tractamento in deviation ab illo al centro del rotation.



The Clinical Evaluation and Management of Radiation Accident Exposure Patients¹

CAPT. E. R. KING, MC, U.S.N.²

IN RECENT YEARS, the danger of peacetime nuclear accidents has become so prevalent that most medical centers are faced with the responsibility of providing for care of individuals exposed to such mishaps. Some major accidents in the United States, or within its testing program (1-4), as well as in foreign countries (5, 6), have already occurred. Radiologists are certain to be consulted on the subject of possible plans or means to care for the victim in such a situation.

The National Naval Medical Center, Bethesda, Md., has been designated as the Radiation Exposure Evaluation Center for the U. S. Navy. In the preparation and planning required for such responsibility, the staffs of the Departments of Radiology and of Nuclear Medicine of that Command have devised a plan whereby, it is believed, persons involved in an ionizing radiation accident, or incident, would receive optimal medical care. The following discussion is a résumé of the present concept of an evaluation program for such cases.

Some definition of terms seems in order. The word "accident" refers to a situation in which personnel are known to be exposed to excessive doses (exceeding the "maximum permissible doses" listed by the National Committee on Radiation Protection) of ionizing radiation which may result from: (a) damage to a nuclear reactor shield, or the reactor fuel container, or the escape of reactor coolant; (b) damage to a nuclear weapon, with resultant escape of nuclear fuel; (c) damage and resultant rupture of a container of a "sealed source" of a radioisotope, such as is used in medicine or industry; (d) a reactor excursion, or "run-away"; (e) accidental exposure to a "beam" of radiation or another source of radiation, be it from a nuclear reactor, a

medical or industrial source of radioactivity, or a radiographic installation (x-ray unit); (f) any other possible excessive exposure.

An "incident" is a situation whereby in any of the above situations, or perhaps in some not listed, personnel might have been exposed but no definite evidence of such exposure can be proved at the site. This latter situation may be very important from a medicolegal standpoint.

PATIENT EVALUATION AT THE EXPOSURE SITE

The Navy has established two Radiation Disaster Teams, the East Coast unit being stationed at the Explosive Ordnance Disposal Center, Indian Head, Md. The medical element of this team, staffed by the National Naval Medical Center at Bethesda, primarily serves in an advisory capacity to the command of the military establishment nearest the accident or incident. In case of an actual accident, possible procedures for this team are as listed in the following table:

TABLE I: PATIENT EVALUATION AT ACCIDENT SITE

- I. Survey of accident site by Radiation Disaster Team; determination of type and severity of accident
- II. Determination of possible types of exposure to individuals in the area
- III. Determination of probable radiation exposure dose
- IV. Segregation and evacuation of known exposure cases
- V. Procurement of positive identification and permanent addresses of individuals at the exposure site whose evacuation was not required. Follow-up studies on these persons are mandatory

Note: In this situation it will be difficult to evaluate the extent of exposure. If

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this is in doubt and the number of persons is small (20 or less), the safest procedure is to evacuate all.

PATIENT EVALUATION AT THE HOSPITAL ADMITTING ROOM

Patients who are evacuated will be transported to the National Naval Medical Center, Bethesda, Md. At this Command a separate ward (Building 110) has been prepared for admission of such cases. The routine to be followed in this building has been described previously (7-9), but we feel it so important that it will be repeated:

TABLE II: ADMISSION ROOM MANAGEMENT OF RADIATION DISASTER VICTIMS

- I. *Ambulatory Patients (Uninjured)*
 1. Monitor patient with clothes on. If he is not obviously contaminated, allow him to leave the area temporarily for later consideration
 2. If contamination is detected, remove and dispose of clothing
 3. Refer patient to decontamination area for thorough washing under shower, with a detergent and scrub brush
 4. Dry in shower room
 5. Monitor outside shower room. If contamination is still present, repeat shower (clip hair, if necessary)
 6. Dress patient in pajamas
 7. Send to area designated by doctor on duty
 8. Make sure the patient is available for further studies indicated by the type of exposure (low background total-body counting, hematological studies, radioassays of excreta, etc.)
- II. *Ambulatory Patients (Injured)*
 1. If patient has first aid or temporary dressings, monitor as though he were uninjured
 2. If further first aid is needed, perform same
 3. If bandages or first-aid dressings that have been applied are soiled, etc., it may be necessary to remove the top layers and monitor as previously stated
 4. If the patient is contaminated, remove his clothes, remonitor, and dress in pajamas. Carry out any emergency treatment required
 5. If the patient is grossly contaminated and could withstand a cleansing shower, perform this procedure, then dress him in pajamas and admit to the hospital. Perform additional studies as indicated by the type of exposure (see I, 8)

III. *Stretcher Patients (Noncritical)*

1. Monitor patient. If he is not contaminated, remove clothing, dress in pajamas, and admit to hospital as a probably non-contaminated person
2. If patient is contaminated, remove clothing, take him to tub sink or tub bath, decontaminate as much as possible, dress in pajamas, and admit to hospital. Perform additional studies as indicated by type of exposure (see I, 8)

IV. *Stretcher Patients (Critical)*

1. Administer necessary first aid
2. Monitor as thoroughly as possible
3. If patient does not appear contaminated, treat as any other non-contaminated, critically injured stretcher patient; then admit to hospital
4. If patient is contaminated and in critical condition, wash surface area as much as possible and admit to hospital. Perform additional studies as indicated by type of exposure (see I, 8)
- V. All representatives of the press will be referred to the Administrative Officer. Patients and attending physicians, nurses and technicians will not be subjected to interviews by the press

PATIENT MANAGEMENT

After the admission procedures, the patients will be managed according to an estimate of the dose of radiation they have received. Ordinarily this estimate would be expected to be available from the Radiation Physicist at the scene of the accident, but, as found by experience with previous peacetime accidents such as the Y-12 accident (4), the complexities of exposure may not permit this. More advanced types of personnel detectors, including varied emulsion film badges and different types of foils for neutron detection, may allow a more accurate estimation than has been possible up to the present time. Actually, dose determination may best be made on the basis of clinical findings, but these would probably take too long to become manifest to be of value in planning therapy in many instances. Nevertheless, the most logical method of making a prognosis in a radiation casualty is by the dose the patient has received, if any reasonable estimate of such dosage is available.

TABLE III: PROGNOSIS FOR PATIENTS EXPOSED TO EXTERNAL RADIATION

- Group I: Survival probable—100–300 rem. Use supportive therapy as indicated. (Probably none will be needed)
- Group II: Survival possible—300–750 rem. Major effort should be devoted to this group
- Group III: Survival improbable—750 rem and upward. This group (750–1,500 rem) may be saved by autologous bone marrow (perhaps homologous also). Doses over 1,500 rem are likely to be fatal
- The rem is used as a dose unit in that the above doses are for all types of ionizing radiation, and are estimates of the absorbed dose of radiation.

These dose estimates are for patients who receive optimal medical care and not for persons exposed under wartime conditions. The latter groups would probably not receive as good medical care and could not withstand the larger doses of radiation. If mass casualties were involved the above doses would be lowered considerably, Group III possibly being as low as 600 rem. It is difficult to ascertain an exact dosage.

As stated above, the dose and prognosis would depend, in part, on the type of accident. Thus, as can be seen in Table IV, a "general" or "induced" type of exposure, or a mixture of these types, would allow a greater volume of tissue to be damaged by absorbed radiation than would a "superficial" exposure.

The problem of the physicist who attempts to determine the patient's dosage is also complicated by the multiple types of exposure that may be involved.

TABLE IV: TYPES OF EXPOSURE

- I. "General" exposure—external type, *i.e.*, gamma, x-ray neutrons. This produces a "general" systemic reaction
- II. "Superficial" exposure—external type, *i.e.*, soft energy gamma or x-ray or beta-particle irradiation. Most of the reaction is "superficial," with little "general" reaction
- III. Induced radiation exposure—external neutrons—Reaction is "general" from radioactivity induced by the neutron flux as well as by the neutron damage to tissues
- IV. Internal contamination. Radioactivity is deposited inside the body

Here, again, a definition of terms seems pertinent. By "general" exposure, we

imply that "general," or systemic reaction would result, with leukopenia, thrombocytopenia, and anemia, in that order. These findings would appear earlier with an increasing dosage of ionizing radiation. Within limits, there seems to be some relationship between the radiation dose received and the appearance of a depression of the hematopoietic system (10). Also, the time of onset of epilation varies with the dose as well as with the energy of the radiation. An acute dose of about 250 to 300 rad of 150 to 175-kev x-ray or gamma-ray irradiation causes temporary epilation, but for Co^{60} irradiation, of slightly over 1 Mev, the acute dose required is between 425 and 450 rad (11). The relationship of the appearance of nausea, vomiting, and diarrhea to the absorbed dose seems to be unresolved; nevertheless, it can be said that these are symptoms resulting from a "general" type of exposure.

On the other hand, the "superficial" types of exposure are due to the less penetrating beta particle, or weak gamma or x-rays, which are absorbed by the superficial layers of the covering of the body. Thus, their effects are quite similar to those of thermal burns.

In "induced" exposures, neutron radiation is added to that previously mentioned. In neutron exposure many of the elements of the body, such as sodium, chlorine, iodine, etc., become radioactive, with the same result as if these radioelements were directly injected. Neutrons, furthermore, are quite destructive. All of this adds up to a complex problem of dosimetry.

Internal contamination is not an acute problem but is quite insidious. By the entry into the body, by any means, of appreciable activity of a tissue-seeking radioelement of long half-life, the critical organ in which such an element is deposited is exposed to an almost constant ionizing assault for many years. Thus, the carcinogenic potentiality of the irradiation is increased. The total activities that appear to be detrimental for the various radio-nuclides are listed in *Handbook 52* of the National Bureau of Standards series (12).

Management of exposed persons will be discussed according to the type of exposure, as well as the Group under which the patient would be listed in Table III. As stated above, information as to the type of accident and of exposure should not be difficult to obtain, but an accurate dosage estimate may be next to impossible. Thus the clinician in charge of the patient must use his own medical judgment. Table V lists a suggested procedure.

TABLE V: "GENERAL" EXPOSURES
("Groups" listed herein refer to Table III)

Early Management

1. Good nursing care: all groups
2. High caloric and protein low-residue diet, with supportive vitamins: Groups II and III
3. Fluid and electrolyte balance maintenance (preferably by oral route): Groups II and III

Late Management (after 14 days, Groups II and III)

1. Meticulous nursing care
2. Adequate diet, modified according to clinical status
3. Continued maintenance of fluid and electrolyte balance (orally, if at all possible)
4. Fresh whole blood, if needed
5. Platelet transfusions if hemorrhagic diathesis is present or imminent
6. Bone-marrow transfusions (or transplants)
7. Antibiotics if indicated

It should be noted that the Group I patients are not included in this table for late management, as they probably will require no special care after two to three weeks post-exposure time.

The assay of urine for certain amino acids appears to afford the most promising indication of the radiation absorbed by the patient. It has been reported (4, 13) that levels of excretion of taurine and BAIBA (beta-aminoisobutyric acid) follow a radiation dosage response. Thus, in all cases aliquots of the twenty-four-hour urines should be preserved for special analysis in an attempt to assist in the establishment of a biochemical dosimeter.

It may be noted that we have substituted the word "management" for "therapy" in much of this discussion. This is because we are still reluctant to speak of specific therapy for these patients. Most of the treatment is supportive; if any specific

therapy were to be offered, it would be in the form of bone-marrow transplants, a procedure which some workers also feel is supportive.

The use of autologous (from the same individual) bone-marrow transplants is very promising, and if a method could be developed to preserve autologous marrow for a prolonged period, it might prove life-saving when radiation disasters occur. Homologous (from another individual, or donor) marrow has not proved as efficacious and there is some doubt as to the authenticity of "takes" of homologous transplants by irradiated patients.

The use of antibiotics is outlined in Table VI. As with most other therapeutic measures, common sense and good judgment are most important in deciding what antibiotics to use and when to use them.

TABLE VI: USE OF ANTIBIOTICS
("Groups" listed herein refer to Table III)

1. Prophylactic use not indicated
2. For Groups II and III culture naso-oro-pharyngeal washings, stools, and urine. Select broad-spectrum antibiotics for pathogens demonstrated
3. When signs and symptoms of infection are present, give large doses of the selected antibiotics
4. For localized infections use customary hot soaks, etc.
5. Mass casualty situation: Do the best you can with what you have

Table VII outlines management of the "superficial" type of radiation damage which is similar to that for thermal burns, usually of first or second degree.

TABLE VII: MANAGEMENT OF "SUPERFICIAL" RADIATION EXPOSURE

1. Good nursing care; sterile technic in dressing areas of vesiculation and weeping
2. Application of bland lotions (non-oil base) to areas of irritation and weeping
3. Débridement when indicated
4. Plastic surgery as indicated
5. Supportive therapy for general systemic reactions; in general, the same as for thermal burns

This exposure may result from rupture of a reactor core or weapons' casings, fall-out, or rupture of sealed sources

Tables VIII and IX refer to more specific measures required for patients exposed to neutrons and/or for those in whose bodies radioactive materials have been deposited.

TABLE VIII: MANAGEMENT OF THE INDUCED RADIATION CASE

- I. If dosage is high, measures listed in Table V may be followed
- II. Adequate measurement of induced radioactivity is necessary, by
 - (a) Whole-body counting
 - (b) Urine, blood, and tissue radioassays

This type of exposure is most likely to occur during a reactor run-away or "excursion"

TABLE IX: MANAGEMENT OF CASES WITH INTERNAL CONTAMINATION

- I. Proper evaluation of circumstances of exposure
- II. Attempts to measure "body burden" (whole-body counting, radioassays of urine, etc.)
- III. Mobilization of contaminants by chelating agents
- IV. Removal of contaminants from blood stream by the artificial kidney (?)

This type of exposure may evolve from ingestion, inhalation, or injection (into wounds, etc.) of radioactive contaminants, resulting from nearly any type of accident.

If a neutron exposure has occurred, it is most likely that there will have been external gamma-ray (photon) exposure as well, and the management would be the same as for the "general" exposure patient.

With induced radiation or internal contamination, certain specific studies should be made that are not required for "general" or "superficial" forms of exposure. These include urine radioassays for induced radioactivity (elements of the body made radioactive by neutron collision, such as Na^{24} , P^{32} , etc.) and determination of excretion of internally deposited contamination (Pu^{239} , Sr^{90} , I^{131} , H^3 , etc.). One of the most important special studies to be performed, as listed in Tables VIII and IX, is the whole-body counting of these patients. By this procedure one can determine the total radioactivity in the body, the types of radioactive materials present, and, quite likely, the organ systems in which this radioactivity has been deposited.

There has been but little discussion of

methods of estimating the radiation dose, although it is recognized that this factor is of primary importance in evaluating and managing radiation disaster patients. It has been pointed out that both the prognosis and the treatment of these cases depend upon the dosage determinations (Table III). Discussion of dosimetry can become very technical and it is not believed such details should be included in a general discussion such as this. It may be stated that, up to the present, attempts to determine radiation dosages received during radiation accidents by physical and electronic methods have not been too satisfactory. Apparently the peripheral blood count, coupled with special biochemical studies of the urine (determination of taurine and beta-amino-isobutyric acid), may prove the best criteria for dose estimation. The patient's clinical signs and symptoms are also of extreme importance.

SUMMARY

A description of a practical approach to the problem of the clinical management of radiation disaster patients has been offered. Important details of this problem involve adequate control of the admission room management, as well as determination of type of exposure and of the radiation dose. Most of the treatment now available is supportive in nature. Good judgment in caring for such cases is of great importance.

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REFERENCES

1. HEMPELMANN, L. H., LISCO, H., AND HOFFMAN, J. G.: Acute Radiation Syndrome: Study of Nine Cases and Review of the Problem. *Ann. Int. Med.* **36**: 279-510, Feb. (pt. 1) 1952.
2. KNOWLTON, N. P., JR., LEIFER, E., HOGNESS, J. R., HEMPELMANN, L. H., BLANEY, L. F., GILL, D. C., OAKES, W. R., AND SHAFER, C. L.: Beta Ray Burns of the Human Skin. *J.A.M.A.* **141**: 239-246, Sept. 24, 1949.
3. CRONKITE, E. P., BOND, V. P., AND DUNHAM, C. L., eds.: Some Effects of Ionizing Radiation on Human Beings. U.S.A.E.C. Washington, D. C., Superintendent of Documents, U. S. Government Printing Office, 1956.
4. BRUCER, M., ed.: A Medical Report on the Y-12 Accident. ORINS-25. Washington, D. C., Office of Technical Services, Department of Commerce, 1959.

5. Accident of Windscale No. 1 Pile. British White Paper. New York, British Information Sales Section, November 1957.
6. MATHÉ, G., JAMMET, H., PENDIC, B., SCHWARZENBERG, L., DUPLAN, J. F., MAUPIN, B., LATARJET, R., LARRIEU, M. J., KALIC, D., AND DJUKIC, Z.: Transfusions et greffes de moëlle osseuse homologue chez des humains irradiés à haute dose accidentellement. *Rev. franç. études clin. et biol.* **4**: 226-238, March 1959.
7. NH BETH Instruction 6470.4 dated March 10, 1959. Bethesda, Md., U. S. Naval Hospital.
8. KING, E. R.: The Management of Victims of a Radiation Accident. *South. M. J.* **53**: 432-440, April 1960.
9. KING, E. R.: Clinical Management of Patients Exposed to Radiation Disasters. Eighth Annual National Medical Civil Defense Conference, A.M.A., Miami Beach, Fla., June 11, 1960.
10. MCFARLAND, W.: Personal communication.
11. Unpublished data.
12. Maximum Permissible Amounts of Radionuclides in the Human Body and Maximum Permissible Concentrations in Air and Water. Handbook 32, National Bureau of Standards, Washington, D. C., Office of Technical Services, U. S. Department of Commerce.
13. CAVALIERI, R. R., VAN METRE, M., CHAMBERS, F. W., AND KING, E. R.: Taurine Excretion in Humans Treated by Total-body Radiation. *J. Nuclear Med.* (In press).

SUMMARIO IN INTERLINGUA

Evaluatione Regime Clinic de Patientes de Accidentes de Radiation

Es describe un procedimento con respecto al regime clinic pro patientes de disastros de radiation. Detalias importante de iste problema es listate in forma de tabellas, incluse le evaluation del patiente al sito del accidente, le tractamento in le sala de admissiones, e le determination del typo e del quantitate de exposition.

Le prognose si ben como le tractamento depende del determinaciones de dosage. Le numeration in le sanguine peripheric, in combination con special studios biochimic del urina (determination de taurina e de acido beta-amino-isobutyric) as apparentemente le melior criterio pro le estimation

del dosage. Le signos e symptomias clinic es etiam importantissime. Technicas suggerite pro expositiones "general" e "superficial" es listate.

Con radiation inducite (in que neutrones es addite a altere expositiones) o contamination interne, certe studios specific debe esser facite le quales non es requirite pro formas "general" o "superficial" de exposition radiational. Istos include le radio-essayage del urina del patientes e contationes a corpore total.

Le tractamento currentemente disponibile es primariamente supportative.



Radiation-Induced Changes in the Gastrointestinal Function of Mice and Their Prevention by Chemical Means¹

EMANUEL E. SCHWARTZ, M.D., and BERNARD SHAPIRO, M.D.

DEATH of rodents during the first week after whole-body or abdominal exposure to 1 to 10,000 r is due mainly to small-bowel injury (1, 2). Among the events which precede death are the mitotic arrest of the crypt cells (1, 3), impairment of DNA synthesis (4, 5), intestinal weight loss (6, 7), alterations in gastrointestinal motility (8), and water and electrolyte imbalance (9, 10). These effects can be prevented, in part, by the administration of certain sulfhydryl compounds shortly before irradiation (11-15).

Studies of the effect of radiation on the normal functions of the gastrointestinal tract, such as digestion and absorption, may provide further insight into the mechanism of injury and death from this cause. Morehouse and Searcy (16) observed that supralethal doses of radiation retard the absorption of dioleypalmitin in rats. Carbohydrate absorption has also been found to be reduced after whole-body x-ray exposure (17, 18).

The purpose of the present investigation was to evaluate the effect of different doses of radiation upon intestinal absorption in mice and to attempt to prevent any impairment by the preadministration of 2-mercaptoethylguanidine (MEG), the transguanylated form of S-(2-aminoethyl)thiuronium bromide hydrobromide (AET). Oleic acid and serum albumin were selected as test substances because the small intestine is the primary site of their absorption. Moreover, the absorption of oleic acid does not depend upon the presence of pancreatic enzymes.

METHODS

Ten-week old male C57BL/6J mice² be-

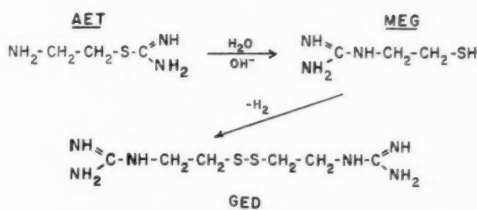


Fig. 1. Transguanylation of S-(2-aminoethyl)thiuronium bromide hydrobromide (AET) to 2-mercaptoethylguanidine (MEG) and oxidation to bis(2-guanidoethyl) disulfide (GED).

tween 18 and 25 gm. were confined in separate sectors of a rotating cylindrical Plexiglas container during whole-body x-irradiation. They were fasted³ for eighteen hours before irradiation in the twenty-four-hour oleic acid experiments, but in the albumin-absorption and the sequential oleic-acid-absorption studies they were fasted for only one hour. Different groups of mice received either 175 mg./kg. intraperitoneally, by mouth, or 400 mg./kg. of MEG (1 mg./0.05 c.c.), or an equivalent volume of sham solution,⁴ ten and thirty minutes, respectively, before irradiation. MEG (pH 7.5) was prepared as described earlier (19). Since MEG is rapidly oxidized in mildly alkaline solutions to bis(2-guanidoethyl) disulfide (GED) (Fig. 1), it was administered within two or three hours of preparation. Irradiation was carried out with the following physical factors: 250 kvp, 30 ma, 0.25 mm. Cu and 1 mm. Al added filtration, 0.95 mm. Cu h.v.l., 74 cm. F.S.D. Dose rates as measured with a calibrated Victoreen ionization chamber immediately before and after each experimental run varied from 89 to 100 r per minute, including backscatter, on different days.

¹ From the Departments of Radiology, Northern and Southern Divisions, Albert Einstein Medical Center, Philadelphia, Penna. Accepted for publication in November 1960.

² This work was sponsored by the United States Atomic Energy Commission, Contract AT(30-1)-2406.

³ Obtained from Jackson Memorial Laboratory, Bar Harbor, Maine.

⁴ These mice had been previously maintained on Purina Laboratory chow.

⁵ This sham solution was comprised of 0.6 c.c. HBr in 100 c.c. of pH 7.5 PO₄ buffer, 0.06 molar.

Oleic-Acid and Serum-Albumin Absorption Studies: Mice were permitted free access to food for thirty hours following irradiation and were then fasted for twenty-four hours. Fifty-four hours after irradiation, each animal was force-fed 0.15 c.c. or 0.25 c.c. of I^{131} -labeled oleic acid⁵ (prepared with carrier oleic acid to give a specific activity of 0.1 μ c/0.20–0.25 c.c.) by means of a 1-c.c. tuberculin syringe and an adapted 20-gauge cannula introduced into the esophagus. This was immediately followed by 0.05 c.c. of a dilute dextrose-protein hydrolysate mixture⁶ to insure complete and rapid passage of the test material to the stomach. Since the same syringe and feeding tip were used for all subjects, special calibrations of the syringes were not performed.

The serum albumin procedure was essentially the same as that for oleic acid, except for the reduction of the fasting period to four hours before administration of albumin, and of the total interval between irradiation and albumin administration to fifty-three hours. I^{131} -labeled human serum albumin⁷ was prepared with carrier human serum albumin as a 5 per cent solution in saline with a specific activity of 0.1 μ c/0.2 c.c. Each animal received 0.15 c.c. of this solution.

Most of the oleic acid recipients were sacrificed after twenty-four hours by cervical dislocation. To determine the sequence of events during this period, mice in other experiments were sacrificed at four, eight, twelve, sixteen, and twenty hours. Serum albumin absorption was measured one hour after feeding the test material. Stomach and intestines (small and large intestines combined) were isolated from the remainder of the gastrointestinal tract with hemostats and, after being freed from adjacent fat and mesentery, were removed together with their contents. Feces were also collected. These samples were wet-ashed by stirring in a warm

mixture of 5 N NaOH in absolute ethyl alcohol for one to two hours. After the sample volumes were brought up to 15 c.c., their radioactivities were determined in a scintillation well counter.⁸ I^{131} activity not found in the gastrointestinal tract or feces was assumed to have been absorbed. Since higher doses of irradiation increased gastric retention, except where otherwise specified absorption was calculated as percentage of test material which actually reached the intestines during the test period, according to Formula 1:

$$\text{Per Cent Absorption} = \frac{\text{Activity Fed} - (\text{Gastric} + \text{Intestinal}) + \text{Fecal Activity}}{\text{Gastric Activity}} \times 100$$

Preliminary studies were performed to confirm the stability of the I^{131} -oleic acid bond and I^{131} -serum albumin bond in the gastrointestinal tract. Chemical analyses of stomach and intestinal contents five hours after oleic acid feeding showed that I^{131} was not removed from the oleic acid during passage through these organs. Thirty minutes after the feeding of serum albumin, they contained some I^{131} as iodide. In experiments in which the pylorus was ligated, however, all of the I^{131} in the stomach contents or wall was found to be bound to the albumin. It was concluded, therefore, that the appearance of I^{131} -iodide in the stomach, and possibly in the intestine as well, resulted from the rapid absorption and metabolism of labeled albumin with redistribution of I^{131} -iodide throughout the body. There was minimal absorption of both oleic acid and serum albumin from the stomach.

Intestinal Weight Determination: Intestinal weight determinations were performed in other mice in a corollary study. These animals were sacrificed fifty-three

⁵ Oleotope. E. R. Squibb & Sons.

⁶ Modified fibrin hydrolysate low sodium mixture (Abbott).

⁷ Albumotope. E. R. Squibb & Sons.

⁸ Sodium iodide crystal, 2-inch outer diameter, with 1 \times 1 1/2 inch well accommodating 15 c.c. volume of liquid for counting.

TABLE I: OLEIC ACID ABSORBED BY INDIVIDUAL IRRADIATED MICE IN TWENTY-FOUR HOURS

X-ray Dose →	0 r		600 r		800 r		1,000 r	
Treatment →	Sham	MEG*	Sham	MEG	Sham	MEG	Sham	MEG
	%	%	%	%	%	%	%	%
	77	92	68	73	61	77	34	78
	81	79	79	70	61	69	47	55
	79	76	76	85	52	77	43	57
	81	75	78	40	37	71	30	78
	81	71	65	65	51	47	14	54
	85	72	68	67	40	51	21	59
	80	69	71	57	62	69	21	58
	83	43	60	66	59	58	20	52
	89	66	92	59	56	82	37	62
	82	66	74	68	56	70	41	62
	81	74	64		70	77	16	56
	94	56	63		67	55	53	60
	90	78	77		62	63	43	54
	63	82	79		52	54	13	52
	84		65		51	78		52
					77	56		
Mean % Absorbed (S.D.)	82.0† (6.7)	71.4 (11.3)	71.9 (8.2)	65.0 (11.1)	57.1 (9.9)	65.9 (10.6)	28.1 (12.9)	59.3‡ (8.0)

* 175 mg./kg. MEG intraperitoneally ten minutes before irradiation.

† The mean absorption of 3 mice exposed to 400 r was 79 per cent.

‡ Differences between groups treated with sham solution and groups treated with MEG prior to 800 r or 1,000 r were highly significant ($P < 0.01$).

TABLE II: SEQUENTIAL OBSERVATIONS FOLLOWING OLEIC ACID ADMINISTRATION*

	Dosage	Hours after Force-feeding				
		4	8	12	16	20
Percentage of fed oleic acid retained in stomach	0 r	38	30	15	8	5
	800 r	74	50	37	35	17
Percentage of fed oleic acid absorbed†	0 r	31	35	49	68	79
	800 r	6	15	18	32	48
Percentage of fed oleic acid remaining in intestines‡	0 r	30	30	34	20	14
	800 r	17	28	39	28	27

* The mean of 4 to 6 mice is listed for each control and irradiated group.

† That is, percentage of fed oleic acid no longer found in gastrointestinal tract or feces (Formula 2):

$$\text{Per cent Absorption} = \frac{\text{Activity Fed} - (\text{Gastric} + \text{Intestinal} + \text{Fecal Activity})}{\text{Activity Fed}} \times 100$$

‡ Radioactivity in the feces of irradiated mice was not significantly greater than in unirradiated controls.

hours after x-ray exposure, and their small intestines were removed, opened longitudinally, and agitated in cold saline to remove adherent food and waste material. The organs were then placed on tared planchets and heated for eighteen hours at 95° C. Following this they were allowed to cool in a desiccator and weighed.

RESULTS

Oleic Acid: Unirradiated mice absorbed an average of 82.0 per cent of the oleic acid reaching the intestines in twenty-four hours. Absorption was reduced to 71.9 per cent after 600 r, to 57.1 per cent after 800 r, and to 28.1 per cent after

1,000 r. Results from individual mice are listed in Table I. The dose-effect relationship was largely eliminated by pretreatment with MEG given intraperitoneally. Absorption in protected mice was 65.9 per cent after 800 r and 59.3 per cent after 1,000 r. MEG itself appeared to have some inhibitory effect on the intestinal absorption of oleic acid in the absence of irradiation.

Gastric retention measured in the same animals was also inhibited by MEG. At the end of twenty-four hours only 3.7 per cent of the administered activity was still present in the stomach of controls, whereas after 1,000 r 39.4 per cent remained.

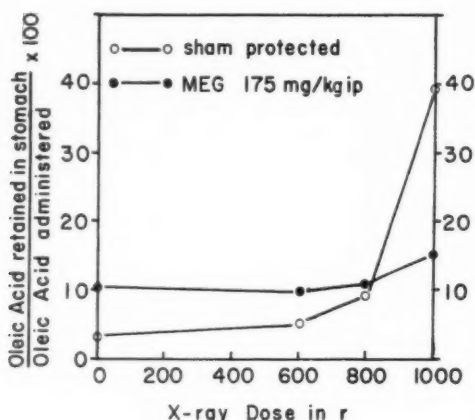


Fig. 2. Twenty-four-hour gastric retention of I^{131} -oleic acid measured fifty-four hours after whole-body irradiation, with and without MEG pretreatment. The means of the gastric retention values of the mice listed in Table I are shown here.

TABLE III: CUMULATIVE OLEIC ACID ABSORPTION*

X-Ray Dose	Pretreatment	4 Hr. (%)	8 Hr. (%)	12 Hr. (%)	16 Hr. (%)	20 Hr. (%)
0 r	Sham	47	49	57	73	82
800 r	Sham	20	31	29	46	60
800 r	MEG†	26	40	60	59	72

* The mean absorption of 4 to 6 mice is listed for each interval. Absorption was calculated by Formula 1.

† Intraperitoneal administration of 175 mg./kg. ten minutes before start of irradiation.

MEG-pretreated irradiated mice had almost normal gastric retention (Fig. 2). The four-hour sequential studies revealed that 800 r also retarded gastric emptying (Table II).

Cumulative intestinal absorption at successive four-hour intervals is recorded for unirradiated animals and for recipients of 800 r, in Table II. A dose of 800 r caused a reduction in the percentage of fed oleic acid absorbed from the gastrointestinal tract at each interval. Despite the increased gastric retention which existed in the 800 r-exposed animals, the oleic acid remaining in their intestines tended to be equal to or greater than that in controls (Table II). Absorption in the irradiated animals was also reduced, as calculated on the basis of the test material actually reaching the intestines (Formula 1). Improved function in MEG recipients was apparent at each time interval (Table III).

MEG (400 mg./kg.) administered orally was somewhat more effective than intraperitoneal MEG (175 mg./kg.) in preserving intestinal absorption after 1,000-r whole-body exposure (Table IV). The increased gastric retention secondary to irradiation was likewise prevented by MEG via this route.

Serum Albumin Studies: Labeled serum albumin was much more rapidly absorbed than oleic acid in both normal and irradiated mice (Fig. 3). Gastric retention increased after higher doses of radiation, as in the case of oleic acid. When absorption was calculated on the basis of activity reaching the intestines (Formula 1), rather than on the basis of activity fed (Formula 2, Table II), it was apparent that there was no decrease in this function during the test

TABLE IV: EFFECT OF ORAL MEG* ON TWENTY-FOUR-HOUR OLEIC ACID ABSORPTION

X-Ray Dose	Pretreatment	Gastric Retention (%)	Absorption† (%)
0 r (14)†	Sham	3.9 ± 2.3	78.2 ± 5.8
1,000 r (15)	Sham	26.9 ± 9.3	42.8 ± 11.8
1,000 r (10)	MEG	6.9 ± 4.4	73.2 ± 7.7

* Administration of 400 mg./kg thirty minutes before irradiation.

† Calculated by Formula 1.

‡ Figures in parentheses show the number of mice tested to obtain the means and standard deviations listed.

period. One-hour absorption, both without irradiation or after as much as 1,400 r, when thus corrected for gastric retention, ranged from 85 to 87 per cent (Fig. 3). Results with 25 per cent serum albumin were similar to those obtained with 5 per cent albumin and are therefore not shown.

Small Intestinal Weight: There was an inverse relationship between weight of the

small intestines and x-ray dose. Intestinal dry weight after 1,200 r was only 59 per cent of normal. Decreases in weight following 800 r and 1,200 r were partially prevented by MEG (Fig. 4). The intestines were also observed to be considerably more friable when mice were sacrificed after these higher doses.

impaired functional capacity following irradiation. We have, therefore, concluded that the decreased absorption as calculated by either Formula 1 or 2 was due to a primary effect on the small bowel.

MEG, in large measure, prevented both radiation-induced changes, *i.e.*, the increased gastric retention and impaired

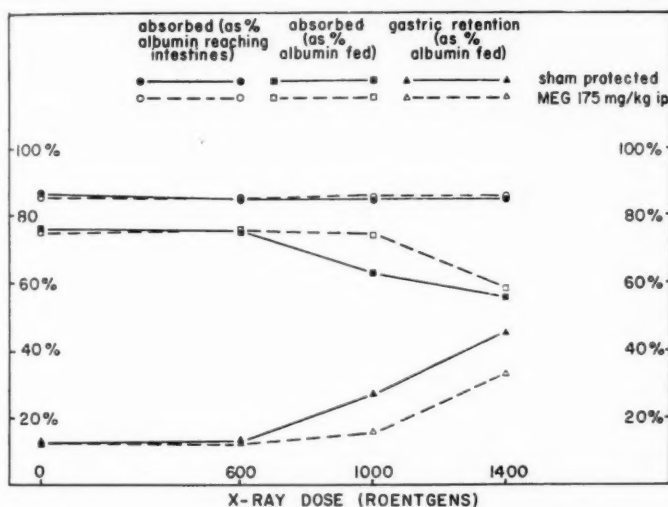


Fig. 3. One-hour I^{131} -serum-albumin intestinal absorption and gastric retention measured fifty-three hours after irradiation, with and without MEG pretreatment. Each point represents an average of 9 to 14 mice.

DISCUSSION

These studies indicate that a decrease in oleic acid absorption as well as a delay in gastric emptying occurs following irradiation with doses of 600 r and above. Since absorption is dependent upon the availability of a substance within the intestines (20, 21), it was necessary to evaluate the influence of the decrease in gastric emptying observed in the above experiments. This was done by measuring gastric retention as well as intestinal absorption in mice exposed to 800 r and in controls at four-hour intervals. The sequential study revealed that there was sufficient fatty acid available for intestinal absorption after 800 r at each interval examined (Table II). It would appear that, despite increased gastric retention after this dose, the amount of oleic acid entering the small intestine exceeded its

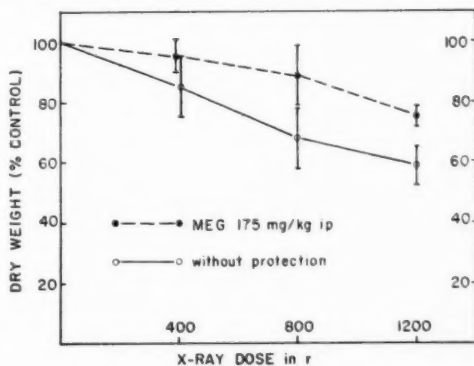


Fig. 4. Intestinal weights in mice fifty-three hours after x-irradiation as compared to those in unirradiated animals, with and without protection. Each point represents the mean of 9 to 10 mice. Standard deviations are represented by brackets.

intestinal absorption of oleic acid. Mice receiving MEG orally prior to 1,000 r had better absorption than did similarly ir-

radiated mice receiving the protective agent parenterally. Since oral recipients of the sham solution before 1,000 r likewise fared better than sham-injected irradiated recipients, and since all mice were fasting, the observed difference may, in part, have been due to the presence of fluid within the gastrointestinal tract. This suggests that a liquid bolus in itself may confer some protection. The slight inhibitory action of intraperitoneal MEG on oleic acid absorption in unirradiated mice after a lapse of fifty-four hours (Table I) cannot be explained at this time.

Approximately 86 per cent of serum albumin was absorbed within one hour in both control and irradiated mice. This rapid absorption probably was not due to the short fasting periods used in the protein experiments, since in other studies, not tabulated, serum albumin was absorbed equally rapidly by mice fasted as long as the oleic acid recipients. It should be noted that the amount of serum albumin administered to each mouse, 7.5 mg., was far less than the amounts of oleic acid fed, 134 or 223 mg. However, 25 per cent serum albumin, *i.e.*, 37.5 mg. per feeding, was absorbed as rapidly as the 5 per cent mixture used in the results presented.

Although serum albumin absorption, as calculated by Formula 2, indicated decreased absorption after large doses of radiation, when gastric retention was considered in the calculation (Formula 1), it was apparent that this finding was not due to decreased intestinal function (Fig. 3). These results indicate that intestinal availability of serum albumin was the major factor limiting intestinal absorption. MEG decreased gastric retention of albumin after irradiation and did not influence the rapid absorption of protein available for absorption in the intestines.

It is difficult to compare the above results with previous studies of intestinal absorption in the post-irradiation state because of variations in technics and timing used. The authors are not aware of

any published report concerning the absorption of protein following irradiation. However, Shishova (22) found that the absorption of amino acid mixtures injected directly into rat small bowel was reduced after 500 to 600 r. Mead and collaborators (23) observed no impairment of methyl oleate absorption in mice after 600 to 700 r. Morehouse and Searcy (16) found that the absorption of fat was markedly reduced two days after 1,000 r and 1,500 r. The importance of the time factor is illustrated by Dickson's (24) finding that there was no decrease in glucose absorption in mice until seventy-two hours after 500 r despite increased glucose retention by the stomach as early as four hours. These results, as well as our own, are in accord with the time sequence of previously reported (1, 3) histologic changes in the intestine after irradiation.

Several technics are applicable to the determination of intestinal absorption. Because of its convenience, a frequently used method is the periodic sampling of blood following ingestion. Blood levels, however, are influenced by metabolism and excretion, in addition to absorption. Moreover, after ingestion radioactivity is relatively low in the blood as compared with the gastrointestinal tract. The latter consideration is especially important in the case of small laboratory animals, such as mice, whose total gastric capacity may be limited to 0.20 or 0.25 c.c.

Protection against whole-body irradiation by 2-mercaptoethylguanidine (MEG) is evidenced by diminished injury of critical tissues such as the small intestine (15) and bone marrow (25), or by survivals after otherwise supralethal irradiation. The reduction of small intestinal weight loss obtained under our experimental conditions (Fig. 4) can be correlated with the absorption studies with regard to both time and dose. Also in keeping with these results is the fact that no unprotected mice have survived in our laboratory seven days after whole-body exposure to 1,000 r, whereas 80 per cent have survived for a period of that length after irradiation

following pretreatment with MEG (175 mg./kg. intraperitoneally).

Since it is now possible to protect against intestinal and hematopoietic tissue injury due to irradiation, two major causes of death after whole-body irradiation can be prevented in lower mammals. Unfortunately, the clinical application of radioprotective chemicals remains limited at this time because of their high degree of toxicity in man (26). It is hoped that studies under way in this and other laboratories will further elucidate the mechanism of protection and toxicity by these agents.

SUMMARY

Whole-body x-irradiation with 600 r and higher doses caused impairment in the intestinal absorption of iodinated oleic acid in mice two days after exposure. Diminution in I^{131} -labeled serum albumin absorption was not observed even after 1,400 r. Although irradiation also caused increased gastric retention, this was apparently not responsible for the decrease in fatty acid absorption. The administration of 2-mercaptoethylguanidine before irradiation, either orally or intraperitoneally, largely prevented the deleterious effect on absorption and gastric emptying. The significance of this functional impairment by irradiation and the preservation of life and function by chemical radioprotective agents are discussed.

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REFERENCES

1. QUASTLER, H.: The Nature of Intestinal Radiation Death. *Radiation Res.* 4: 303-320, April 1956.
2. BOND, V. P., SWIFT, M. N., ALLEN, A. C., AND FISHLER, M. C.: Sensitivity of Abdomen of Rat to X-Irradiation. *Am. J. Physiol.* 16: 323-330, May 1950.
3. MONTAGNA, W., AND WILSON, J. W.: A Cytologic Study of the Intestinal Epithelium of the Mouse After Total Body X-Irradiation. *J. Nat. Cancer Inst.* 15: 1703-1736, June 1955.
4. NYGAARD, O. F., AND POTTER, R. L.: Effect of X-Radiation on DNA Metabolism in Various Tissues of the Rat. I. Incorporation of C^{14} -Thymidine into DNA During the First 24 Hours Postirradiation. *Radiation Res.* 10: 462-476, April 1959.
5. SHERMAN, F. G., AND QUASTLER, H.: DNA Synthesis in Irradiated Intestinal Epithelium. *Exper. Cell Res.* 19: 343-360, March 1960.
6. CONARD, R. A.: Dose Dependence and Sequential Changes in Mouse Small Intestinal Weight Induced by Ionizing Radiation. *Proc. Soc. Exper. Biol. & Med.* 86: 664-668, August-September 1954.
7. KAY, R. E., AND ENTENMAN, C.: Weight, Nitrogen and DNA Content of Small Intestine Mucosa of Rats Exposed to X-Rays. *Am. J. Physiol.* 197: 13-18, July 1959.
8. CONARD, R. A.: Effect of X-Irradiation on Intestinal Motility of the Rat. *Am. J. Physiol.* 165: 375-385, May 1, 1951.
9. BOWERS, J. Z., DAVENPORT, V., CHRISTENSEN, N., AND GOODNER, C. J.: Effects of Acute Whole-Body X-Irradiation on Salt and Water Metabolism and Their Clinical Significance. *Radiology* 61: 97-101, July 1953.
10. JACKSON, K. L., RHODES, R., AND ENTENMAN, C.: Electrolyte Excretion in the Rat After Severe Intestinal Damage by X-Irradiation. *Radiation Res.* 8: 361-373, April 1958.
11. GEREBTZOFF, M. A., AND BACQ, Z. M.: Pathology of Mice Irradiated After Injection of Cysteamine (β -Mercaptoethylamine). [In] Second Radiobiology Symposium, Liège, ed. by Z. M. Bacq. London, Butterworth, 1955, p. 290.
12. MAISIN, H., AND FIÉVÉ, C.: Étude histologique de la réparation intestinale chez des rats irradiés sous diverses conditions de protection. [In] Second Radiobiology Symposium (see 11), London, Butterworth, 1955, pp. 304-309.
13. MOLE, R. H., AND TEMPLE, D. M.: Intestinal Damage by Radiation and Its Chemical Modification. *Nature, London* 180: 1278, Dec. 7, 1957.
14. BELILES, R. P., KERELAKES, J. G., AND KREBS, A. T.: Influence of Cysteine on the Intestinal Epithelium of X-Irradiated Rats. *J. Nat. Cancer Inst.* 22: 1045-1057, June 1959.
15. MAISIN, J. R., NOVELLI, G. D., DOHERTY, D. G., AND CONGDON, C. C.: Chemical Protection of the Alimentary Tract of Whole-Body X-Irradiated Mice. I. Changes in Weight, Histology, and Cell Division in Relation to Nucleic Acid and Protein Synthesis. *Internat. J. Radiation Biol.* 2: 281-293, July 1960.
16. MOREHOUSE, M. G., AND SEARCY, R. L.: The Effects of Irradiation on the Absorption and Distribution of Dioleypalmitin- C^{14} in the Rat. *Radiation Res.* 4: 175-185, March 1956.
17. FARRAR, J. T., SMALL, M. D., BULLARD, D., AND INGELFINGER, F. J.: Effect of Total Body Irradiation on Absorption of Sugars from the Small Intestine. *Am. J. Physiol.* 186: 549-553, September 1956.
18. MOSS, W. T.: The Effect of Irradiating the Exteriorized Small Bowel on Sugar Absorption. *Am. J. Roentgenol.* 78: 850-854, November 1957.
19. SCHWARTZ, E. E., AND SHAPIRO, B.: The Protection of Mice Against Radiation by 2-Mercaptoethylguanidine and Its Disulfide. *Radiation Res.* 13: 768-775, November 1960.
20. THOMAS, J. E.: Mechanics and Regulation of Gastric Emptying. *Physiol. Rev.* 37: 453-474, October 1957.
21. GOODMAN, R. D., LEWIS, A. E., AND SCHUCK, E. A.: Effects of X-Irradiation on Gastrointestinal Transit and Absorption Availability. *Am. J. Physiol.* 169: 242-247, April 1, 1952.
22. SHISHOVA, O. A.: The Effect of Ionizing Radiation, Adrenalectomy, and Cortisone Treatment on the Intestinal Absorption of Amino Acids. *Biochimiiia (Moscow)* 24: 812-817, 1959.

23. MEAD, J. F., DECKER, A. B., AND BENNETT, L. R.: Effect of X-Irradiation upon Fat Absorption in the Mouse. *J. Nutrition* **43**: 485-499, April 1951.

24. DICKSON, H. M.: Effect of X-Irradiation on Glucose Absorption. *Am. J. Physiol.* **182**: 477-478, September 1955.

25. URSO, P., CONGDON, C. C., DOHERTY, D. G., AND

SHAPIRA, R.: Effect of Chemical Protection and Bone Marrow Treatment on Radiation Injury in Mice. *Blood* **13**: 665-676, July 1958.

26. CONDIT, P. T., LEVY, A. H., SHNIDER, B. I., AND OVIEDO, R. G.: Some Effects of S,2-Aminoethylisothiuronium Bromide Hydrobromide (AET) in Man. *Cancer* **13**: 842-849, July-August 1960.

SUMMARIO IN INTERLINGUA

Alterationes Inducite per Radiation in le Function Gastrointestinal de Muses, e le Prevention de Illos per Medios Chemic

Roentgeno-irradiation del corpore total con doses de 600 r e plus causava in muses un defecto in le absorption intestinal de iodate acido oleic duo dies post le exposition. Nulle reduction del absorption de albumina seral a marcation con I^{131} esseva notate mesmo post un dosage de 1400 r. Ben que le irradiation causava etiam un augmento del retention gastric, isto non pareva esser responsabile pro le reduce

absorption de acido grassiose. Le administration de 2-mercaptoethyl-guanidina ante le irradiation—per via oral o per via intraperitone—preveniva in grande misura le effectos adverse in le absorption e in le vacuation gastric.

Es discutite le signification de iste dysfunction causate per irradiation e del preservation de vita e function per chemic agentes radioprotectori.



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Effect of Irradiation to Adrenal Upon Circulating Adrenal Medullary Hormone in the Rat¹

M. G. GRIFFITH, J. Q. GRIFFITH, JR., M.D., M. B. HERMEL, M.D., and J. GERSHON-COHEN, M.D.

IN A PREVIOUS study (1), we described the effect of irradiation to the adrenal of the rat upon the level of blood corticosterone, especially after stimulation by ACTH injection. The irradiated animals showed a lower level of this adrenal cortical hormone than did the controls. This study has now been extended to the adrenal medullary hormones. While it is known that the adrenal medulla is relatively resistant to irradiation (2), at least as compared with the cortex, so far as we are aware, no experimental series has been followed with studies of these hormones after irradiation.

Weil-Malherbe and Bone (3, 4) have described a method for measuring epinephrine-like substances in the blood, as well as a procedure for evaluating epinephrine and norepinephrine by means of differential filters and a suitable calculation. We planned to repeat, as closely as possible, the program of the earlier cortical study except that, since the amount of blood required entailed the sacrifice of the animal, only one measurement could be made per rat. This was done under ether anesthesia, which is known to increase slightly the amount of circulating adrenal medullary hormone (5). A further modification was undertaken after the first four animals that were sacrificed failed to show any difference between the irradiated and non-irradiated pair. This consisted in the injection of insulin prior to sacrifice in an attempt to raise medullary hormone level, as described elsewhere (6, 7).

MATERIALS AND METHODS

Measurement of epinephrine-like substances in the blood was carried out by the method of Weil-Malherbe and Bone

(3), as adapted by Persky and Roston (8) to the Farrand photoelectric fluorometer, which we also used, though Weil-Malherbe and Bone did not. The formula of Weil-Malherbe and Bone (4) was used, however, for the calculation of epinephrine and norepinephrine.

By insertion of a needle into the abdominal aorta of the anesthetized rat as much blood was removed as possible. The syringe was moistened with sodium fluoride-sodium thiosulphate solution, as recommended by Weil-Malherbe and Bone, and quickly emptied into a measuring cylinder containing 5.0 ml. of the same solution. The volume of blood averaged 7.5 ml. but was actually measured in the cylinder, and the final calculation was corrected for the actual volume.

There were two series of experimental animals. The first consisted of 42 females, weighing 200 grams \pm 10 grams, from which the left adrenals had been removed surgically four days prior to irradiation. Of these, 21 received irradiation to the right adrenal, the factors being as follows: 90 kv; 5 ma; target-skin distance 11.5 cm.; added filter 1 mm. Al; h.v.l. 2.2 mm. Al; r/min. 333; circular field 3 cm. in diameter. Eleven rats received 500 r to the right adrenal, and 10 rats received 1,000 r. No anesthetic was used, but during irradiation the rat was immobilized with multiple tapes to a restraining board.

The first 4 rats of this series were sacrificed four weeks after irradiation. Following this, it was decided, as mentioned above, to employ insulin stimulation of the medulla in the remaining rats just prior to sacrifice.

The second series of 10 rats, similar in age, weight, and sex to the first series but without prior adrenal operation or irradiation,

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TABLE I: TOTAL FLUORESCENCE OF EPINEPHRINE AND NOREPINEPHRINE EXPRESSED AS EPINEPHRINE (Gamma per Liter)

Number of Rats	Unilateral Adrenalectomy	Irradiation	Insulin	Median	Arithmetical Mean	Standard Deviation
5	0	0	0	14.7	18.0	6.9
5	0	0	+	29.0	33.9	14.1
19	+	0	+	27.2	31.0	11.3
10	+	500 r	+	28.0	33.7	16.3
9	+	1000 r	+	40.3	39.0	17.2

TABLE II: EPINEPHRINE AND NOREPINEPHRINE BLOOD LEVELS (Gamma per Liter)

Number of Rats	Unilateral Adrenalectomy	Irradiation	Insulin	Epinephrine			Norepinephrine		
				Median	Arithmetical Mean	Standard Deviation	Median	Arithmetical Mean	Standard Deviation
5	0	0	0	9.1	10.0	4.0	18.5	16.0	3.1
5	0	0	+	22.3	31.7	15.8	10.5*	11.4*	4.3*
16	+	0	+	22.2	24.0	9.6	14.9	16.6	8.8
7	+	500 r	+	16.7	20.2	9.4	20.3	16.6	8.5
7	+	1000 r	+	22.4	27.5	14.7	16.4	15.9	7.1

* Based upon 4 rats only.

tion, were then used to study the effect of insulin alone upon circulating adrenal medullary hormone. The dose selected, 1/4 unit added to 1.0 c.c. of distilled water and given intraperitoneally one hour prior to sacrifice, was known in our animals to produce a marked hypoglycemia. This amount was given to 5 of the 10 rats, while the others received the distilled water alone.

Following completion of the insulin study, the remaining 38 rats from the first series were sacrificed during the next three weeks, or within seven weeks of the time of irradiation, each being given insulin. The animals were sacrificed in groups of 4 or 6 each, equal numbers of controls and irradiated animals being included in each working period.

RESULTS

The 4 rats sacrificed four weeks after irradiation showed the following values (all in gamma per liter): (1) Epinephrine-equivalent, 30.2 and 15.8 for the controls and 28.1 and 16.4 for the low- and high-dose irradiated animals respectively. (2) Epinephrine, quantitated in only 3 rats, was 10.2 for the controls, and 28.1 and

11.5 for the low- and high-dose irradiated rats, respectively. (3) Norepinephrine could be quantitated in only 2 rats, being 17.1 for a control and 14.7 for a high-dose irradiated rat. These values are not included in Tables I and II.

Table I lists the epinephrine-equivalent values for 48 rats, including 38 from the first series and 10 from the second series. The values in Table II represent the same animals provided results could be quantitated as epinephrine and norepinephrine—a total of 40 rats.

Insulin, as expected from the literature (6, 7), appears to increase the circulating epinephrine-like substances, due primarily to an increase in epinephrine itself. The irradiated rats show levels of circulating epinephrine-like substance, epinephrine, and norepinephrine no lower than those of the non-irradiated controls.

DISCUSSION

The actual levels of adrenal medullary hormones in the blood found in this study are higher than those reported elsewhere. Aronow *et al.* (9), who used a pooled blood specimen and the method of Weil-Malherbe and Bone, found 9.6 gamma

per liter of epinephrine and 4.3 gamma per liter of norepinephrine in the "stressed cardiac" female rat (for the stressed guinea-pig they found 38.8 and 53.0 gamma per liter of epinephrine and norepinephrine respectively). They did not use insulin as a medullary hormone stimulant, but Bethune *et al.* (6), who did, found a seventy-fold increase in epinephrine and a five-fold increase in norepinephrine in the adrenal venous blood of dogs following the intravenous injection of crystalline insulin.

In the present study, interpretation of results would be essentially the same whether based upon the epinephrine-like levels or the epinephrine and norepinephrine levels. That the latter is subject to some criticism must be admitted, this being well summarized by Valk and Price (7), who point out that the fluorescence (norepinephrine) condensate decays exponentially and irreversibly in strong blue or green light, which is necessary to the partition. They state that a substance present in plasma and interfering in their (EDT) method may be dopac. Dopac is biologically inactive, but its fluorescence ratio differs from that of norepinephrine by less than 10 per cent.

The method used, therefore, would seem to be more accurate for epinephrine than for norepinephrine.

SUMMARY

Irradiation to the adrenal in the rat in

doses of 500 and 1,000 r does not lower the level of circulating adrenal medullary hormone, as determined after stimulation by ether anesthesia and insulin injection. This is, therefore, confirmation of the observation based upon histologic studies, that the adrenal medulla is more resistant to irradiation than is the cortex.

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REFERENCES

1. GRIFFITH, M. G., GRIFFITH, J. Q., JR., HERMEL, M. B., AND GERSHON-COHEN, J.: Effect of Irradiation to Adrenal Upon Circulating Adrenal Cortical Hormone in the Rat. *Radiology* **76**: 110-112, January 1961.
2. HOLLAENDER, A., ed.: *Radiation Biology*. Volume I. High Energy Radiation. New York, McGraw-Hill Book Co., Inc., 1954, p. 991.
3. WEIL-MALHERBE, H., AND BONE, A. D.: Chemical Estimation of Adrenaline-Like Substances in Blood. *Biochem. J.* **51**: 311-318, June 1952.
4. WEIL-MALHERBE, H., AND BONE, A. D.: On the Occurrence of Adrenaline and Noradrenaline in Blood. *Biochem. J.* **58**: 132-141, September 1954.
5. HAMELBERG, W., SPROUSE, J., MAHAFFEY, J. E., AND RICHARDSON, J. A.: Plasma Levels of Epinephrine and Norepinephrine—Anesthetic Significance. *J.A.M.A.* **172**: 1596-1598, April 9, 1960.
6. BETHUNE, J. E., GOLDFIEN, A., ZILELI, M. S., AND DESPOINTE, R. H.: Effect of Hypoglycemia and Amphenone on Adrenal Secretion of Epinephrine and Norepinephrine. *Fed. Proc.* **16**: 11, March 1957.
7. VALK, A. DE T., JR., AND PRICE, H. L.: Chemical Estimation of Epinephrine and Norepinephrine in Human and Canine Plasma. I. A Critique of the Ethylenediamine Condensation Method. *J. Clin. Invest.* **35**: 837-841, August 1956.
8. PERSKY, H., AND ROSTON, S.: The Quantitative Determination of Adrenaline and Noradrenaline in Mixtures. *Science* **118**: 381-382, Oct. 2, 1953.
9. ARONOW, L., HOWARD, F. A., AND WOLFF, D.: Plasma Epinephrine and Norepinephrine Content in Mammals. *J. Pharmacol. & Exper. Therap.* **116**: 1-2, January 1956.

SUMMARIO IN INTERLINGUA

Le Effecto de Irradiation Adrenal Super le Circulante Hormon Adrenomedullari in le Ratto

In un studio parallel a un altere, previe-mente publicate, in re le effecto de irradiation adrenal super le circulante hormon adrenocortical in le ratto, le autores ha cer-cate determinar le effecto de irradiation adrenal super le circulante hormon adreno-medullari. Studios esseva effectuate in 42 rattos in que adrenalectomia unilateral habeva essite executate quatro dies ante le irradiation. Dece-un del animales recipeva allora 500 r al remanente adrenal e dece recipeva 1000 r. Le alteres remaneva sin

irradiation. In le majoritate del rattos, insulina esseva administrate pro stimular le production de circulante substantias epine-phrinoide.

Esseva trovate que le irradiation del adrenal in le doses usate non reduceva le nivello del circulante hormon adrenome-dullari, determinate post stimulation per (1) anesthesia o (2) insulina. Isto confirma le observationes histologic que le medulla adrenal es plus resistente contra le effectos de irradiation que le cortice.

Radiosensitivity of Malignant Round-Cell Rhabdomyosarcoma in the Nasal Fossa of a Child¹

JEROME M. VAETH, M.D., and THOMAS H. PIATT, M.D.

RHABDOMYOSARCOMAS of the nasal cavity in childhood are rare. Of the 167 rhabdomyosarcomas in children reported by Stout (4), only 3 were primary in the nasal cavity, the nasopharynx being the more common site.

Fifteen cases of embryonal rhabdomyosarcoma arising in cervical, facial, and orbital musculature were reported from the New York Memorial Hospital by Stobbe and Dargeon (3), in patients ranging in age from sixteen months to sixteen years. In 1948 Cappell (1) described 3 such tumors in children, arising beneath the mucous membrane in the uvula and palate. Treatment consisted of local radium application and surgery but was of no avail. All patients had local recurrences and ultimately died with distant metastases in lymph nodes and lungs.

Dargeon (2) has stated that rhabdomyosarcoma is radiosensitive but recurs after radiotherapy. Because of the rarity of this type of neoplasm and the paucity of knowledge of its radioresponsiveness, we are reporting a case in a young girl, arising in the nasal fossa, with histologically verified metastases in the cervical lymph nodes. This tumor, although unusually radiosensitive both at the primary and secondary sites, ultimately recurred and the patient died with pulmonary metastases.

CASE REPORT

An 8-year-old Caucasian girl was admitted to the University of California Medical Center (San Francisco) on Jan. 6, 1960, with a history of recurrent episodes of right nasal bleeding since June 1959. In August 1959, there had been discovered a polypoid pink-gray mass on the right nasal fossa floor, extending along the nasal septum posteriorly to the entrance of, but not into, the nasopharynx. The tumor was removed surgically at that time and was histologically reported as "chronic granulation tissue." Two months later a recurrence at the



Fig. 1. Paranasal roentgenogram before roentgen therapy.

same site was removed (October 1959) by the same surgeon. The child was then referred to the University of California Medical Center for further treatment.

On admission to this hospital, the right nostril was completely obstructed by a fleshy, red, polypoid tumor which extended through the right choana into the vault of the nasopharyngeal cavity. The left nasal fossa was not unusual. Otoscopic examination showed a fluid level on the right associated with diminished hearing on that side. Several enlarged, firm, tender lymph nodes were palpable in the right midcervical area under the sternocleidomastoid muscle. The left cervical lymph nodes were also slightly enlarged. The remainder of the physical examination was not significant. The child's birth, development, and past history were normal.

The results of laboratory studies were normal. Roentgenograms showed a density in the right nasal fossa and nasopharynx (Fig. 1) and opacification of both maxillary antra. No bone destruction was seen. There was no abnormality apparent on the chest film.

Radical eradication of the tumor was considered justified if it proved to be confined to the primary site and the adenopathy represented inflammatory disease. On this basis, several of the enlarged right cervical lymph nodes were removed, as was a biopsy specimen from the right nasal fossa. The lymph

¹ From the Department of Radiology, University of California, School of Medicine, San Francisco, Calif. Accepted for publication in December 1960.

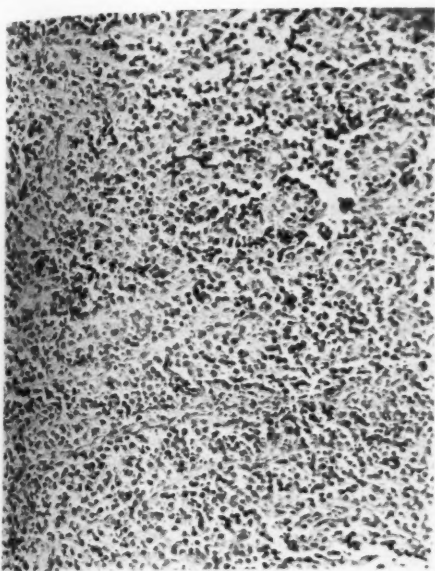


Fig. 2. Photomicrograph of biopsy specimen. Hematoxylin-eosin.

nodes were found to be involved by malignant neoplasm, identical with that at the primary site. The slides of both primary tumor and metastatic nodes were reviewed by Dr. Arthur Purdy Stout (4), who concluded that the tumor was a malignant round-cell rhabdomyosarcoma of childhood ("sometimes called juvenile alveolar rhabdomyosarcoma because the tumor produces pseudo-alveoli") (Fig. 2).

On Jan. 14, 1960, supervoltage external roentgen therapy was begun on the 1-Mev Maxitron (3 ma, no added filtration, h.v.l. 3.2 mm. lead, F.S.D. 70 cm.). The treatment was completed on March 25, after a total of seventy-one days. Initially, in order to evaluate the radioresponsiveness of this neoplasm, a single anteroposterior field measuring 3.5×5.5 cm., encompassing the right nasal fossa, the septum, and minimally the left nasal fossa, was used; the eyes were shielded. The dose was calculated 3 cm. deep from the alae nasi. Within eight treatment days (six treatments, 975 r tissue dose at 3 cm.), the mass in the nasal fossa had diminished by a third of its original size. A tumor was no longer visible in the nasopharynx.

In the meantime, the bilateral cervical adenopathy had increased. Therapy to the upper cervical lymph nodes was then begun with the intention of irradiating the remaining bilateral cervical node chains. By the time 500 r/skin had been delivered to the lymph node areas (while the nasal fossa field was still being irradiated), the left cervical nodes were no longer palpable; the nodes on the right were half their pre-irradiation size.

Radiation therapy to the nasal fossa was com-



Fig. 3. Paranasal roentgenogram, following roentgen therapy.



Fig. 4. Roentgenogram of the chest, six months after roentgen therapy, showing pulmonary metastases.

pleted on Feb. 24, 1960, when a dose of 4,500 r/skin (3,750 r tumor dose) had been delivered in forty-two days. The tumor had regressed completely, and paranasal roentgenograms revealed clearing of the previously reported opacification (Fig. 3). Treatment of the bilateral cervical lymph node chains was accomplished, with delivery of 5,000 r to the midplane of the neck in forty-eight days. Only a small movable right cervical lymph node, less than 1 cm. in diameter, was palpable at completion of therapy. There was a mild skin reaction, consisting of light pigmentation. Epipharyngeal and hypopharyngeal reactions were minimal, never reaching membrane formation. The roentgenogram

of the chest at completion of treatment was normal. Hemoglobin had increased from 12.9 grams (per 100 ml.) at initiation of therapy to 15.0 grams at its completion. The white blood count, differential count, and platelet count showed little change. The child's weight at beginning and end of therapy was 110 kilos (50 pounds).

Within six months after initiation of radiation therapy the tumor had recurred both at the primary site and in the cervical lymph node areas, in spite of the presumably adequate dose. Pulmonary metastases were demonstrable on roentgenograms at the same time (Fig. 4). Death occurred in August 1960. Permission for a postmortem examination was not granted.

SUMMARY

A report of a malignant round-cell rhabdomyosarcoma in the nasal fossa of a

child, with metastases to the cervical lymph nodes, is presented. Both primary and metastatic tumors were extremely radioresponsive but recurred despite thorough irradiation in the treated areas within six months.

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REFERENCES

1. CAPPELL, D. F.: Tumours of Striated Muscle. *Ann. Roy. Coll. Surgeons England* 2: 80-92, February 1948.
2. DARGEON, H. W.: Tumors of Childhood. New York, Paul B. Hoeber, Inc., 1960.
3. STOBBE, G. D., AND DARGEON, H. W.: Embryonal Rhabdomyosarcoma of the Head and Neck in Children and Adolescents. *Cancer* 3: 826-838, September 1950.
4. STOUT, A. P.: Personal communication.

SUMMARIO IN INTERLINGUA

Radiosensibilitate de Maligne Rhabdomyosarcoma a Cellulas Ronde in un Puerio

Es reportate un maligne rhabdomyosarcoma a cellulas ronde in le fossa nasal de un puerio de octo annos de etate. Le patiente esseva primo vidite per le autores con un carnose tumor polypoide de color rubie que se extendeva via le choana dextere ad in le volta del cavitate nasopharyngee. Le massa esseva recurrente post duo operationes in le curso del precedente sex menses. Su natura maligne esseva provate al biopsia, e therapia a radios X de super-

voltage esseva instituite. Le tumor primari dispaveva promptemente, e al tempore del completion del irradiation solamente un micre movibile nodo cervical remaneva palpabile. Intra sex menses il habeva recurrentias tanto al sito primari como etiam in le area del cervical nodo lymphatic. Morte ab metastases pulmonar sequeva intra un anno post le discoperta original del tumor e octo menses post le institution del roentgeno-therapia.



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Benign Subpleural Lymph Node Appearing as a Pulmonary "Coin" Lesion¹

HARRY B. GREENBERG, M.D.

A PERIPHERAL, pulmonary lymph node large enough to appear on chest roentgenograms as a coin lesion is unique. The pulmonary lymph nodes are situated in the parenchyma of the lung adjacent to the larger bronchi and tend to lie in the angles between the bronchial branches, usually extending only as far peripherally as the third bronchial branching. Most lymph tissues found beyond this point consist simply of aggregations of lymphoid cells and can not be regarded as normally occurring structures or true lymph nodes. They are generally caused by a response of the lymphoid tissue to infections, in-

halation of irritating substances, or other noxious stimuli (1, 2).

Miller, in his text on *The Lung*, (1) noted a definite increase in the pulmonary lymphoid tissue of older persons and attributed much of this increase to prior inhalation of carbon or other irritating particles rather than to past infections. The hyperplastic subpleural lymph node in the following case probably represents such a lymphatic response to the inhalation of anthracotic particles. This benign peripheral node appeared on the scout chest roentgenograms as a noncalcified, noncavitary, solitary pulmonary nodule.

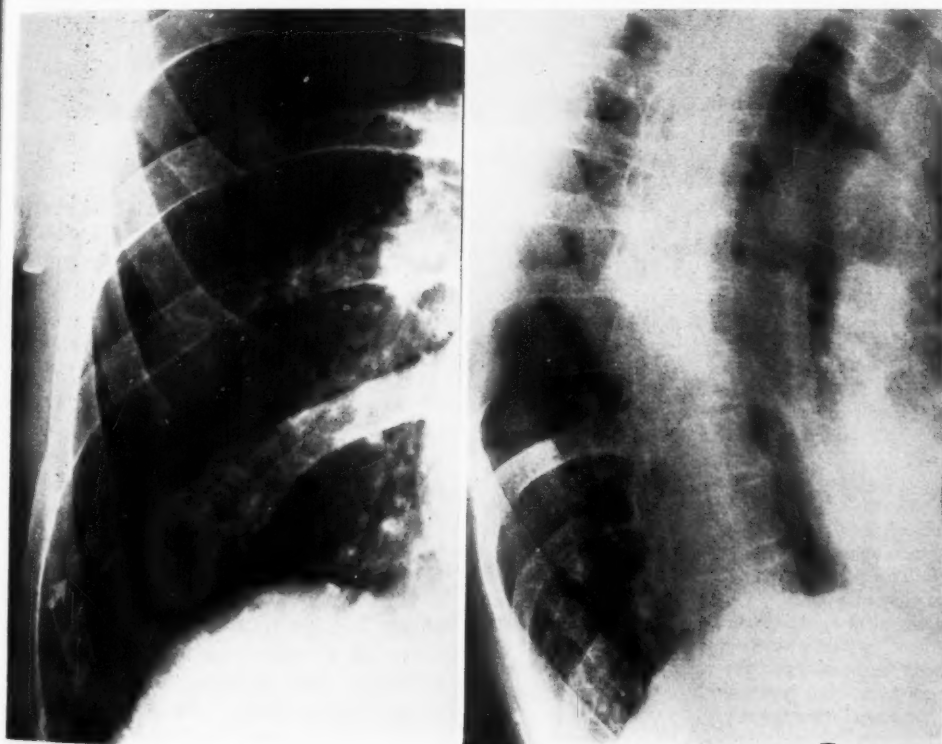


Fig. 1. Postero-anterior and right anterior oblique views showing coin lesion representing a subpleural lymph node.

¹ From the Department of Medicine, Toussaint Infirmary, New Orleans, La. Accepted for publication in November 1960.

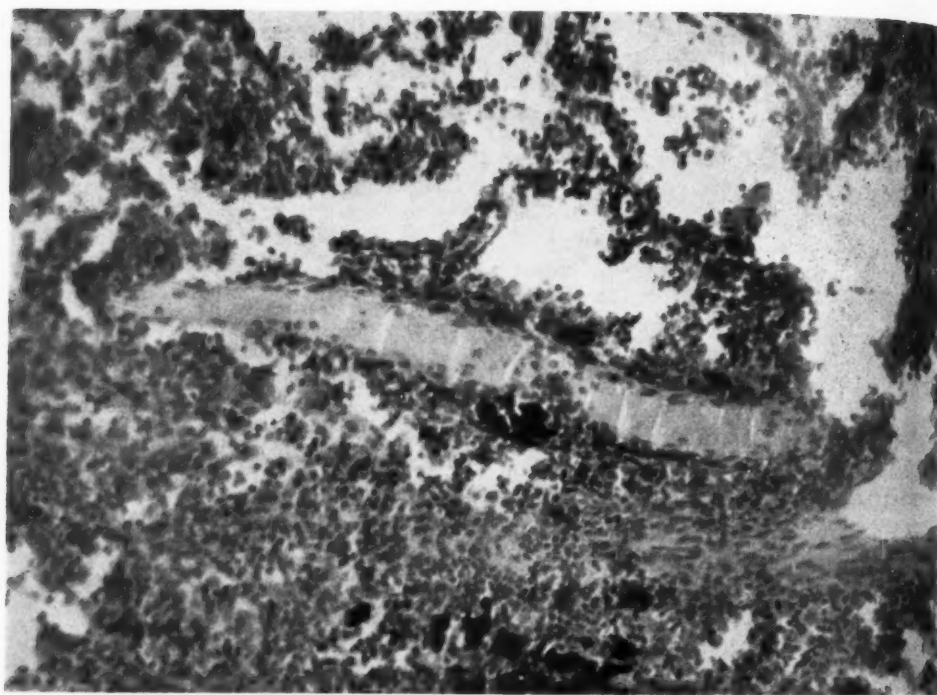


Fig. 2. Section through excised subpleural lymph node showing large amount of anthracotic pigment. Hematoxylin and eosin. $\times 135$.

CASE REPORT

Mr. S. A., a well developed 58-year-old office worker, was hospitalized on Dec. 10, 1959, because of persistent epistaxis following an upper respiratory tract infection. Hemostasis was obtained by the insertion of anterior and posterior nasal packs, and the bleeding did not recur.

Chest roentgenograms made on admission (Fig. 1) revealed a discrete, circumscribed area of increased density, 1.2 cm. in diameter, without calcification or cavitation, situated in the lateral basal segment of the lower lobe of the right lung. There was a calcific infiltrate in the right upper lobe. The patient gave a history of a chronic nonproductive cough often interrupting his sleep. He stated that he habitually smoked one and one-half packs of cigarettes daily.

Physical examination of the chest was negative. There was slight digital clubbing. Intradermal tests with blastomycin and coccidioidin antigens and sputum examinations and cultures for *M. tuberculosis* were negative.

A surgical consultation was obtained and a thoracotomy was recommended. It was subsequently performed without difficulty. A sharply defined, apparently encapsulated tumor, 1.2 cm. in diameter, was resected. Microscopic examination showed the subpleural mass to be a well circum-

scribed, hyperplastic lymph node with a rim of cortical follicles and a medullary portion containing a large amount of carbon pigment (Fig. 2).

COMMENT

In this patient the peripheral, pulmonary lymph node probably became hyperplastic in response to the presence of anthracotic particles. The hazard of carcinoma in the pulmonary coin lesion, particularly in men past the age of forty, has necessarily resulted in the resection of benign, asymptomatic lesions discovered on scout chest roentgenograms (3-5). Granulomas are the most common of these benign entities, though localized areas of chronic pneumonitis, pulmonary infarcts, and benign tumors have also been resected (6-9). Although many diagnostic aids are now available, determination of the exact nature of a pulmonary coin lesion still frequently depends on resection and microscopic examination of the resected specimen (10).

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SUMMARY

A large, hyperplastic, anthracotic, subpleural lymph node appeared on the chest roentgenograms as a noncalcified, pulmonary coin lesion. Exploratory thoracotomy and resection of the lymph node were necessary to establish this unusual diagnosis.

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REFERENCES

1. MILLER, W. S.: *The Lung*. Springfield, Ill., Charles C Thomas, 1947, 2nd ed., p. 138.
2. SHANKS, S. C., AND KERLEY, P., eds.: *A Text-Book of X-Ray Diagnosis*. Philadelphia, W. B. Saunders Company, 1950, 2d ed., Vol. II, p. 270.
3. BOUCOT, K. R., HORIE, U., AND SOKOLOFF, M. J.: Survival in Lung Cancer. *New England J. Med.* **260**: 742-746, April 9, 1959.
4. PAULSON, D. L.: The Importance of the Pulmonary Nodule. *Minnesota Med.* **39**: 127-136, March 1956.
5. HOLIN, S. M., DWORK, R. E., GLASER, S., RIKLI, A. E., AND STOCKLEN, J. B.: Solitary Pulmonary Nodules Found in a Community-Wide Chest Roentgenographic Survey. A Five-Year Follow-up Study. *Am. Rev. Tuberculosis* **79**: 427-439, April 1959.
6. PERKINS, R. B., AND BRADSHAW, H. H.: Pulmonary Infarction Mistaken for Bronchogenic Carcinoma. *J.A.M.A.* **151**: 545-548, Feb. 14, 1953.
7. FLICK, J. B.: Symposium on Surgical Diagnosis; Pulmonary Lesions Simulating Primary Carcinoma of the Lung. *S. Clin. North America* **30**: 1559-1572, December 1950.
8. PAUL, R.: Pulmonary "Coin" Lesion of Unusual Pathology. *Radiology* **75**: 118-120, July 1960.
9. DAVIS, E. W., PEABODY, J. W., JR., AND KATZ, S.: The Solitary Pulmonary Nodule; A Ten-Year Study Based on 215 Cases. *J. Thoracic Surg.* **32**: 728-770, December 1956.
10. UMIKER, W. O.: Diagnosis of Bronchogenic Carcinoma; An Evaluation of Pulmonary Cytology, Bronchoscopy and Scalene Lymph Node Biopsy. *Dis. of Chest* **37**: 82-90, January 1960.

SUMMARIO IN INTERLINGUA

Benigne Nodo Lymphatic Subpleural, con le Apparentia de un Lesion "Monetiforme" Pulmonar

Un grande, hyperplastic, anthracotic nodo lymphatic subpleural appareva in le roentgenogramma thoracic de un masculo de 58 annos de etate como un non-calcificate lesion monetiforme pulmonar. Thoracotomia exploratori e resection del nodo lymphatic esseva necessari pro establir iste

inusual diagnose. Ben que multe adjutas diagnostic es hodie a nostre disposition, le determination del exacte natura de un lesion monetiforme pulmonar continua depender frequentemente de resection e de examine microscopic del reseccate specimen.



Diverticulosis of the Appendix¹

SEYMOUR FISKE OCHSNER, M.D.

DIVERTICULOSIS of the vermiform appendix of the colon is encountered infrequently in roentgenographic study of the intestinal tract. Whether discovery of these diverticula is important has yet to be determined. It is conceivable, however, that they might have clinical significance. It seems reasonable, therefore, for radiologists to keep this entity in mind and to mention its discovery with at least as much care as that accorded to diverticula in other portions of the alimentary canal.

This report concerns two cases in which diverticula of the appendix were visualized in the course of radiologic examination of the colon by barium enema. The first was in a 51-year-old Negro mortician, referred for care because of addiction to Demerol, of two years duration. He had had numerous symptoms for which complete evaluation was undertaken. On roentgenologic examination the colon appeared normal except for three well defined diverticula arising from the mid portion of the appendix (Fig. 1). Appendectomy was not deemed advisable.

The second patient, a white salesman, aged fifty years, was examined at the Ochsner Clinic because of recurring abdominal pains and diarrhea. The only positive physical abnormalities discovered were pronounced diverticulosis of the colon, involving all segments, and a solitary diverticulum arising from the appendix near its base (Fig. 2). Treatment with a low-residue diet resulted in improvement of symptoms.

DISCUSSION

In 1936, Collins (2) presented an extensive historical study of diverticula of the appendix. In the world's literature he found reports of 67 cases, to which he added 30 personal examples that had been discovered in the course of study-



Fig. 1. Three diverticula of appendix revealed in roentgenogram made after barium-enema study.

ing 4,071 appendices after surgical resection or at necropsy. The sex incidence was essentially similar and the average age at the time of discovery was thirty-six years. In 60 per cent of the cases a solitary diverticulum was discovered. In 73 per cent the diverticula were located on or beside the mesenteric border of the appendix. Associated disease was frequent: acute appendicitis in 60 per cent, chronic appendicitis in 33 per cent, perforation of the appendix in 28 per cent, and mucocele or pseudomyxoma peritonei in 20 per cent. These data would seem to indicate that diverticulosis of the appendix is a finding that the radiologist should stress.

Few instances of roentgenographic visualization have been recorded. In 1926, Spriggs and Marxer (11) reported 6 cases in which appendiceal diverticula had been

¹ From the Department of Radiology, Ochsner Clinic, New Orleans, La. Accepted for publication in December 1960.

visualized; their report includes an illustration of a diverticulum of a retrocecal appendix. Kadrnka and Sarasin (7) recorded 2 more cases in 1932, one a solitary appendiceal diverticulum in a patient with ulcerative colitis and the other an instance of multiple appendiceal and cecal diverticula. In the first report in the American literature, Gilmore and Mahan (5) made a preoperative diagnosis of diverticula of the appendix on the basis of visualization during a barium-enema examination. In 1947, Maissa (8) reported a case of solitary diverticulum of the appendix discovered radiographically in a patient with ileocecal tuberculosis. Grout's (6) report of diverticula of the large bowel in 1949 included an illustration of a case in which a diverticulum was discovered in a patient suspected clinically of having chronic appendicitis.

Three additional single cases were recorded in 1957: one by Weiner and Jenkinson (12), who considered the finding unimportant, another by Friedmann (4), who believed the lesion should be recorded because of its rarity, and the third by Salvioni and Elkin (9), who thought the diagnosis was significant and believed that the diverticula in their patient might have been the source of intermittent intestinal bleeding.

In textbooks of radiology, an occasional case is mentioned. Buckstein (1) included an illustration of an appendiceal diverticulum and described it simply as "an unusual anomaly of the appendix." In 28,000 examinations, Feldman (3) reported discovering one case, which he used as an illustration. Shanks (10) wrote that he had seen "one case, found in a normal appendix during a routine examination." These 17 cases are the only reports of roentgenologic diagnosis of diverticula of the appendix that could be discovered in the literature.

SUMMARY

Diverticulosis of the vermiform appendix is relatively infrequent. When it does occur, it may be important because of the



Fig. 2. A large solitary appendiceal diverticulum revealed in a post-evacuation roentgenogram.

frequent association with acute or chronic inflammatory disease, the tendency to easy perforation of the appendix, and the relatively high incidence of pseudomyxoma peritonei. Occasionally, these diverticula may be demonstrated by radiologic study. The radiologist should be alert to this possibility and carefully describe the finding in his report.

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REFERENCES

1. BUCKSTEIN, J.: *The Digestive Tract in Roentgenology*. Philadelphia, J. B. Lippincott Co., Ed. 2, 1953, p. 745.
2. COLLINS, D. C.: Diverticula of the Vermiform Appendix. A Study Based on Thirty Cases. *Ann. Surg.* **104**: 1001-1012, December 1936.
3. FELDMAN, M.: *Clinical Roentgenology of the Digestive Tract*. Baltimore, Williams and Wilkins Co., Ed. 4, 1957, pp. 552-553.
4. FRIEDMANN, A. B.: Diverticula of the Appendix. A Case Report. *Radiology* **68**: 86, January 1957.

5. GILMORE, J. H., AND MAHAN, T. K.: A Case of Diverticulosis of Vermiform Appendix Roentgenographically Demonstrated. *Am. J. Roentgenol.* **56**: 748-750, December 1946.

6. GROUT, J. L. A.: Diverticulosis and Diverticulitis of the Large Intestine (A Radiological Commentary). *Brit. J. Radiol.* **22**: 442-448, August 1949.

7. KADRKA, S., AND SARASIN, R.: A propos de deux cas de diverticules appendiculaires. Examen radiologique. *Bull. et mém. Soc. de radiol. méd. de France* **20**: 321-325, June 1932.

8. MAISSA, P. A.: Diverticulosis del apéndice.

Prensa méd. argent. **34**: 1710-1712, September 5, 1947.

9. SALVIONI, D., AND ELKIN, M.: Diverticula of the Vermiform Appendix. *New York State J. Med.* **57**: 2681-2683, Aug. 15, 1957.

10. SHANKS, S. C.: [In] *Textbook of X-ray Diagnosis*, edited by Shanks and Kerley. Philadelphia, W. B. Saunders Co., Ed. 2, 1950, Vol. III, p. 329.

11. SPRIGGS, E. I., AND MARKER, O. A.: Intestinal Diverticula. *Brit. M. J.* **1**: 130-134, Jan. 23, 1928.

12. WEINER, M. E., AND JENKINSON, E. L.: Diverticula of the Appendix. A Case Observation. *Am. J. Roentgenol.* **78**: 679-680, October 1957.

SUMMARIO IN INTERLINGUA

Diverticulosis del Appendice

Diverticulosis del appendice vermiforme es relativamente infrequente. Quando illo occurre, illo pote esser importante a causa de su frequente association con acute o chronic morbo inflammatori, le tendentia de un preste perforation del appendice, e del relativamente alte incidentia de associate

pseudomyxoma peritoneal. Occasionalmente tal diverticulos pote esser demonstrate per medios radiologic. Es reportate duo casos in que diverticulos del appendice esseva discoperite in le curso de un examine del colon a clyster de barium. Le radiologo deberea esser conscie de iste possibilitate.



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Gas in the Portal Venous System¹

PHILLIP B. SISK, M.D.

IN THE PAST the visualization on a roentgenogram of a branching gas pattern overlying the liver shadow has usually been assumed by the radiologist to be indicative of gas in the biliary tree due to biliary fistula or other biliary tract disease. In recent years, however, there have appeared two reports of gas in the portal venous system, a condition which roentgenographically closely mimics gas in the bile passages. Wolfe and Evans (4) first reported the condition in 1955. They had a series of 6 cases in infants. All were proved at autopsy, and in 4, roentgenograms showed the gas pattern. More recently Susman and Senturia (3) described the first case in an adult and suggested a criterion for differentiating gas in the portal vein from gas in the biliary tree roentgenographically.

The purpose of this paper is to evaluate further the criterion of Susman and Senturia and to report 3 more cases in which gas was demonstrated in the portal venous system.

Susman and Senturia state that gas in the biliary tree is limited to the larger central radicles while gas in the portal venous system fills the finer radicles extending outward nearly to the liver capsule. For this they offer the logical explanation that filling of the biliary tree by gas is hindered by the constant centripetal flow of bile, while filling of the portal venous system is enhanced by the centrifugal flow of blood.

In order to validate this criterion, a number of portal venograms and T-tube cholangiograms done in this department have been analyzed. While these examinations are not directly analogous to gas embolization, it was nevertheless felt that positive results would lend credence to the criterion previously mentioned.

The outcome of this study tended to confirm the hypothesis. In no instance of biliary tract opacification (T-tube cholangiogram) did the opaque substance come closer than approximately 2 cm. to the liver capsule, as visualized on an antero-posterior film. All of the normal portal venograms on the other hand revealed the opacified venous radicles extending outward almost to the capsule (Fig. 1). The only exceptions to this finding were in patients with severe liver disease and portal hypertension (e.g., cirrhosis) with very poor filling of the intrahepatic portion of the portal vein.

CASE REPORTS

CASE I: J. S., a 19-year-old white female, inmate of a state hospital for mental defectives, was referred to the Indiana University Medical Center because of abdominal distention. She had been given prostigmine, Demerol, and oxygen by the referring physician. She was herself unable to give any information.

Physical Findings: The patient appeared critically ill, and the initial examiner recorded "phenomenal abdominal distention." The abdominal wall was so extremely taut that palpation of abdominal contents was not possible. The remainder of the physical examination was not remarkable except for spastic quadriplegia. A Levin tube was passed and approximately 250 c.c. of bloody fluid was obtained.

Roentgen Findings: A postero-anterior chest film revealed marked elevation of the diaphragm, due to the abdominal distention, with no free air beneath. Supine anteroposterior and lateral views of the abdomen showed pronounced gaseous distention probably due to a gas-filled viscus. Very little small bowel was seen. Air in veins throughout the abdominal cavity was noted. The impression of the radiologist at the time was that this represented a distended hollow viscus, probably stomach, and that the condition was most likely due to superior mesenteric artery thrombosis. A second consideration was cecal volvulus (Fig. 2).

Operative Findings: Upon opening the abdomen, a distended hollow viscus appeared through the incision. This was at first thought to be colon but following decompression was seen to be stomach.

¹From the Department of Radiology, Indiana University Medical Center, Indianapolis, Ind. Accepted for publication in November 1960.

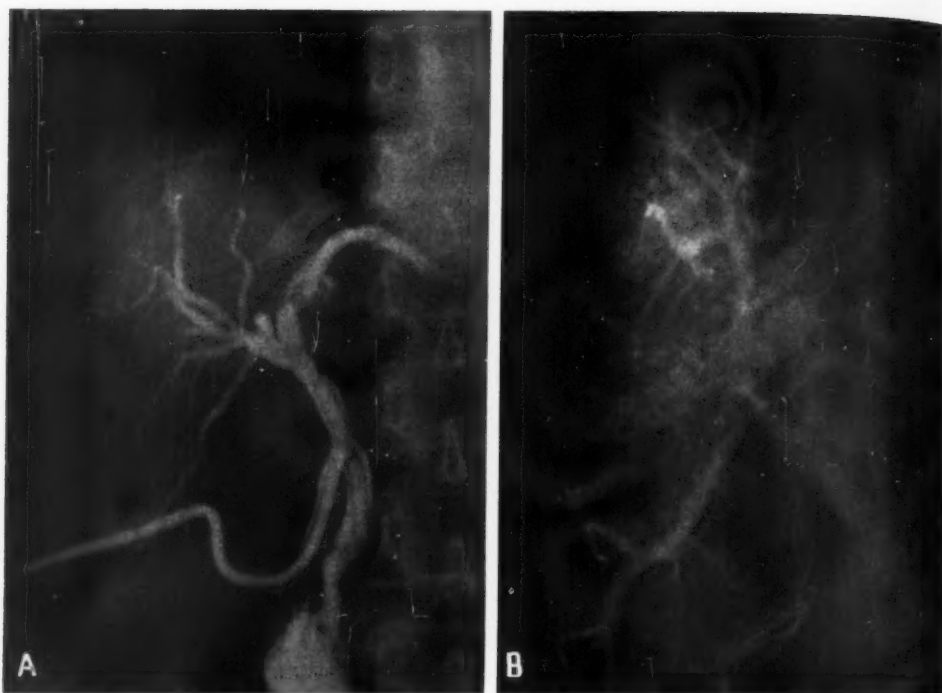


Fig. 1. A. Typical T-tube cholangiogram demonstrating the absence of visible bile ducts in the extreme periphery of the liver.

B. Normal portal venogram demonstrating small venules in the outermost portion of the liver, in contrast to the findings in A.

Many of the abdominal vessels were found to contain more air than blood. The distention of the stomach and duodenum ended abruptly at the superior mesenteric artery. The jejunum, ileum, and colon were not distended. The patient died during the procedure; an attempt at cardiac massage was unsuccessful.

Autopsy Findings: (1) Acute hemorrhagic pancreatitis involving the tail of the pancreas. (2) Extreme dilatation of the stomach and duodenum. (3) Gas within the mesenteric and portal venous system.

CASE II: S. R., an 81-year-old white female, inmate of a mental hospital, was referred to the Indiana University Medical Center because of abdominal distention and vomiting of two days duration. She was unable to give any history.

Physical Findings: The patient appeared to be senile, dehydrated, and acutely ill. The chest was increased in the anteroposterior diameter and hyperresonant to percussion. The heart was slightly enlarged, and a grade-2 systolic murmur was heard over the precordium. The abdomen was distended and tympanitic. Bowel sounds were hypoactive, and occasional high-pitched metallic sounds were heard. No organs or masses were palpated and there was no

tenderness. Soft brown feces were found in the rectum.

Roentgenographic Findings: A postero-anterior chest film revealed pulmonary emphysema with some fibrotic changes. The heart did not appear enlarged. An abdominal film showed two segments of distended small bowel in the left mid-abdomen. No gas was seen in the colon. There was a branching gas pattern in the right upper quadrant, which the radiologist at that time attributed to gas in the biliary system. A rounded density in the right upper quadrant was thought to represent a biliary calculus. A barium enema disclosed no obstruction. The radiologist's opinion was probable mechanical small-bowel obstruction. The presence of the gas in the right upper quadrant led him to suggest the possibility of a gallstone ileus (Fig. 3).

Operative Findings: Exploration revealed incarceration of a loop of ileum and the appendix in the obturator fossa. The tip of the appendix and the loop of bowel were gangrenous. There was no evidence of biliary fistula. Approximately 2 inches of ileum and the appendix were resected. The patient apparently did well for several days postoperatively but abdominal distention again developed, with vomiting. Death occurred seven days after surgery.

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Autopsy Findings: (1) Purulent peritonitis. (2) Bilateral hydrothorax. (3) Acute cholecystitis with hydrops of the gallbladder and multiple small pigment stones. (4) Partial gangrene of practically the entire small bowel (probably due to mesenteric vein phlebitis). (5) Centrilobular necrosis of the liver.



Fig. 2. Case I: Gas within the portal and mesenteric veins secondary to massive dilatation of the stomach and duodenum, which are seen to fill the entire abdomen. The duodenal obstruction was caused by the superior mesenteric artery syndrome.

CASE III: C. W., an 84-year-old white male, was admitted to the Indiana University Medical Center because of a sore foot and pain in the chest. The foot lesion had started as a dermatitis three weeks prior to admission and had progressed to ulceration, which failed to heal. The night prior to admission the patient had experienced sharp pain in the anterior chest, on the right side, which was worse with inspiration. He had had a cough for several years. One year prior to admission he had undergone a transurethral resection of the prostate and bilateral orchiectomy for prostatic carcinoma.

Physical Findings: On examination the patient had a temperature of 99.8° and appeared moderately ill. Examination of the head and neck was not remarkable. The heart was regular and no murmurs were heard. Inspiratory and expiratory wheezes were audible throughout the chest. A pulsatile mass was palpated in the abdomen. The prostate felt hard and the testes were absent. An ulcer was noted over the right ankle.

Hospital Course: The patient was treated with



Fig. 3. Case II: Gas within the portal vein presumably secondary to the distended loop of small bowel seen in the left mid-abdomen. The small bowel obstruction was due to incarceration of a gangrenous loop of ileum in the obturator fossa.

penicillin for his presumed pneumonia, which was verified by a chest film, and was afebrile within twenty-four hours. One week after admission he complained of vague abdominal cramping pain, anorexia, and nausea. Because of this, an upper gastrointestinal series was done, with essentially normal findings. Two weeks after admission the abdominal pain became worse, with distention, tympanites, and high-pitched tinkling bowel sounds. Several hours later, when the abdomen had become silent, a Levin tube was inserted and an abdominal film obtained. In spite of the vigorous medical therapy which was then instituted, the patient's condition rapidly deteriorated and he died within a few hours.

Röntgen Findings: The abdominal film, obtained a few hours before death, showed residual barium from the upper gastrointestinal series of four days previously. There was rather marked dilatation of the small and large bowel, with some fluid levels noted on the decubitus film. A branching gas pattern was present over the liver. The opinion of the radiologist at this time was paralytic ileus and air in the portal venous system of unknown origin (Fig. 4).

Autopsy Findings: (1) Bronchopneumonia, right upper lobe. (2) Arteriosclerosis. (3) Advanced necrosis of the proximal 130 cm. of the jejunum. (4) Dilatation of the aorta. (5) Carcinoma of the prostate.



Fig. 4. Case III: Gas within the portal vein secondary to small bowel gangrene. Note the gas pattern over the liver, extending outward nearly to the capsule, and the marked gaseous distention of the bowel. The barium is residual from an upper gastrointestinal series four days earlier.

DISCUSSION

The etiology of portal-vein gas is unknown. It has been found in several diverse and unrelated conditions—superior mesenteric artery syndrome, mesenteric thrombosis, intestinal obstruction, gastroenteritis, and erythroblastosis fetalis (3, 4). Under all of these conditions there was gaseous distention of the small intestine, which has led some persons to postulate that the gas in the portal vein is a gaseous embolus arising in the intestinal lumen. If this be true, it is reasonable to presume that damage of the bowel wall must also be present in order to facilitate the permeation of the gas through the mucosa, since in several of the cases the degree of small bowel distention was no more marked than is very frequently seen in intestinal obstruction without gas in the portal vein. This was true in several previously recorded cases (3, 4) and 2 of the 3 cases reported above. It has also been postulated that portal

vein gas is an agonal change which is most likely due to a gas-producing infection. There was no definite evidence in support of this theory in any of the reported cases and the apparent rarity of the condition casts some doubt on its likelihood.

Since the finding of gas in the portal vein is such an ominous prognostic sign (all of the reported cases have terminated fatally), its roentgenographic differentiation from biliary tract gas is important. The visualization of gas in peripheral small radicles of the liver (*i.e.*, the outermost 2 cm.) is presumptive evidence of portal-vein gas and should lead to the radiographic and surgical consideration of the diseases which are known to cause this condition.

SUMMARY

1. Three cases of gas within the portal vein visualized roentgenographically are reported.
2. A criterion for differentiation of gas in the portal vein and gas in the biliary tract is evaluated and felt to be valid and helpful. This rule can be summarized as follows: a branching gas pattern over the liver which extends nearly to the liver capsule (*i.e.*, within 2 cm.) is presumptive evidence of gas in the portal vein.
3. The etiology of gas in the portal venous system is discussed briefly.

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REFERENCES

1. DOEHRER, G. A., RUZICKA, F. F., HOFFMAN, G., AND ROUSSELOT, L. M.: The Portal Venous System: Its Roentgen Anatomy. *Radiology* **64**: 675-689, May 1955.
2. SHANKS, S. C., AND KERLEY, P., EDs.: A Text-book of X-ray Diagnosis by British Authors. Vol. III. Abdomen. Philadelphia, W. B. Saunders Co., 3d ed., 1958.
3. SUSMAN, N., AND SENTURIA, H. R.: Gas Embolization of the Portal Venous System. *Am. J. Roentgenol.* **83**: 847-850, May 1960.
4. WOLFE, J. N., AND EVANS, W. A.: Gas in Portal Veins of Liver in Infants: Roentgenographic Demonstration with Post-mortem Anatomical Correlation. *Am. J. Roentgenol.* **74**: 486-489, September 1955.

SUMMARIO IN INTERLINGUA

Gas in le Systema Venose Portal

Es reportate tres casos de visualisation roentgenographic de gas intra le vena portal.

Es evalutate un criterio—valide e utile in nostre opinion—pro le differentiation de gas in le vena portal ab gas in le tracto biliari. Iste regula pote esser summarisate sequentemente: Un configuration ramificate de gas supra le hepate que se extende quasi usque ad le capsula del hepate (i.e.,

usque ad intra 2 cm ab illo) es un indication presumptive de gas in le vena portal.

Le etiologia de gas portal non es cognoscite. Illo ha essite trovate in association con varie conditiones non interrelationate—syndrome del arteria mesenteric superior, thrombosis mesenteric, obstruction intestinal, gastroenteritis, e erythroblastosis fetal. Omne le casos reportate se ha terminate mortalmente.



Radiographic Identification of Arthrogryposis Multiplex Congenita in Utero¹

BERNARD S. EPSTEIN, M.D.

ARTHROGRYPOSIS multiplex congenita (multiple congenital rigid joints; amyoplasia congenita; myodystrophia fetalis deformans) is a condition characterized by varying degrees of joint contractures attributed to the effects of a dystrophic muscular disorder of unknown origin. Disturbances in the spinal cord, notably deficiency of anterior horn cells in the lumbosacral segments, indicate a possible central nervous system component. The interference with joint mobility is due to increased periarticular fibrous tissue. The skin and subcutaneous tissues are sometimes affected, but bone seems to escape except in so far as it is influenced by the muscular, cutaneous, and presumed central nervous system changes. Associated congenital malformations of the skull and spine, polydactyly, and hip dislocation are frequent concomitants. A hereditary factor may exist.

The newborn infant with this condition characteristically presents relatively slender extremities with prominent joints fixed in flexion, extension, or both. Muscle weakness with hypotonia is attributed to loss of striated fibers and replacement by endomysial connective tissue. This is seen more often in the extensor groups (1, 2).

It appears that the abnormal fixation and attitude of the extremities might provide a diagnostic clue on pelvimetric or abdominal roentgenograms.

CASE REPORTS

CASE I. Baby B. was delivered by cesarean section from a mother in whom a polyhydramnios had been present for about two months. Abdominal roentgenograms a week before delivery revealed a single fetus in vertex presentation, with the head hyperextended. The vertebral column appeared intact, but it was noted that the legs were hyperextended on the thighs and that the thighs were flexed

on the abdomen. The significance of this observation was not recognized prior to delivery. The maternal pelvic inlet was quite small, and cephalopelvic disproportion was diagnosed both clinically and radiologically.

After delivery, it was apparent that the infant had arthrogryposis multiplex congenita and a spina bifida occulta with lumbosacral myelomeningocele. Radiographic examination revealed widening of the lumbosacral neural canal, with normal vertebral bodies. A flat soft-tissue mass about 4 cm. in diameter corresponded with the myelomeningocele. The acetabular rims were elevated, and both hips were dislocated upward and laterally. The legs were fixed in the position noted on the prepartum roentgenograms, but the bones of the lower extremities were not otherwise remarkable; the muscular components appeared reduced in size and were streaked with radiolucent areas believed to represent fatty infiltration. The patient was sent elsewhere for surgical treatment of the myelomeningocele.

CASE II. Baby S. was the first child of a 29-year-old woman in whom polyhydramnios was recognized about two months before delivery. The patient was delivered with considerable difficulty and sustained a third-degree pelvic laceration because the lower extremities of the fetus were rigidly flexed on its abdomen, with almost completely fixed joints. The infant survived only a few hours. Roentgenograms demonstrated the changes incident to arthrogryposis. While viewing these films, it was remarked that the condition could have been recognized *in utero* if films had been obtained. Thereupon, one of the house officers recollected that the patient had been in the emergency room about two weeks before because of an automobile accident. The report at that time indicated that no skeletal abnormality was observed and that the distal femoral epiphyses were visible.

On review of the previous abdominal roentgenograms, the upper extremities could not be made out clearly. The flexion of the thighs and the hyperextension of the legs corresponded almost exactly with the postmortem roentgenograms (Fig. 1). The thorax, vertebral column, and pelvis were normal. The acetabular sockets presented a prominent upward angulation with no evidence of dislocation of the hips. The bony architecture of the femurs, legs, arms, and forearms was not remarkable, although the bones appeared rather slender (Fig. 2). The skull was of average size, but the suture lines were

¹ From the Department of Radiology, The Long Island Jewish Hospital, New Hyde Park, N. Y. Accepted for publication in December 1960.

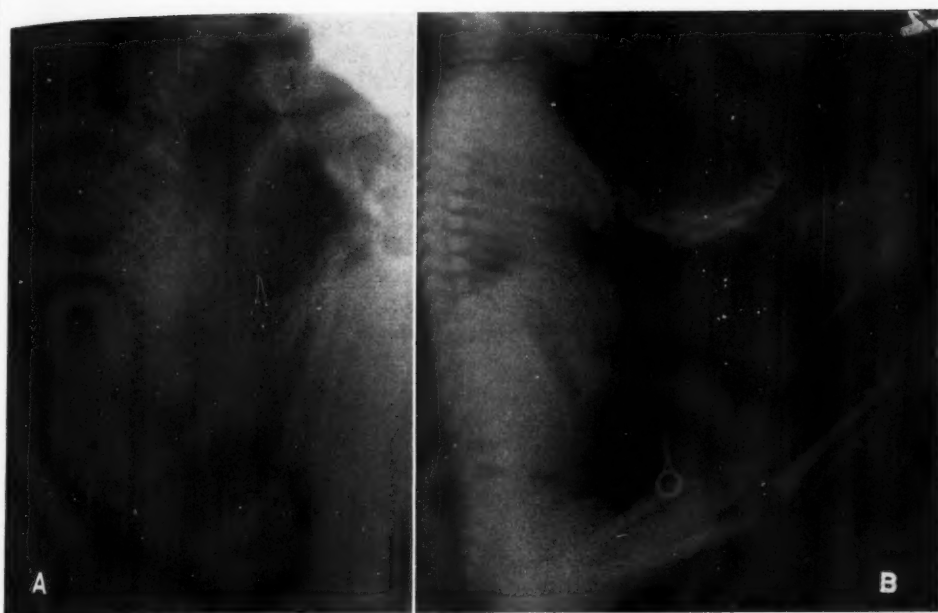


Fig. 1. Case II. A. Prepartum lateral abdominal roentgenogram showing full-term fetus in vertex presentation. Note the hyperextension of the lower extremities. The distal femoral epiphyses are shown.

B. Lateral roentgenogram made immediately after the patient expired. The position of the lower extremities corresponds almost exactly to those on the prepartum roentgenogram.

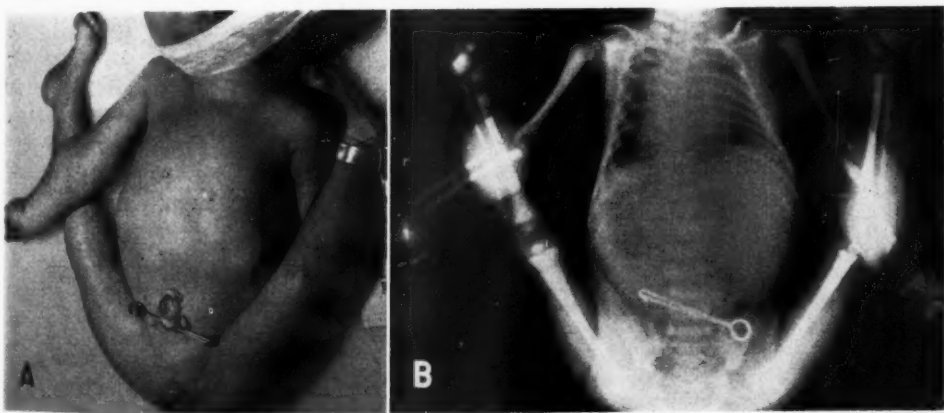


Fig. 2. Case II. A. Photograph of infant. The upper and lower extremities are hyperextended. The fingers and toes are hyperflexed, and the hips are fixed in flexion.

B. Roentgenogram of infant in same position as Figure 2A.

more closely approximated and the fontanelles smaller than normal.

Necropsy disclosed a well nourished infant, with considerable cyanosis of the face, neck, and upper thorax. The genitalia were normal for a newborn female. The anus was perforate. All four extremities were deformed due to immobility of most of the joints, which were quite prominent. The hair over the lower extremities was unusually long and silky.

The elbows were fixed in extension, and both wrists in hyperextension. The fists were edematous, with the fingers firmly in hyperflexion. Both hips were fixed in hyperflexion, the knees and ankles were rigidly hyperextended. Both feet were edematous and the toes were hyperflexed. On dissection, the muscles were found to be infiltrated with fat, and in some areas were replaced by fibrous tissue which presented a pale gray discoloration. This was most

apparent in the thighs and arms. The muscles of the neck, thorax, and abdomen were not remarkable in color or gross architecture.

SUMMARY

Arthrogryposis multiplex congenita may sometimes be identified on prepartum abdominal roentgenograms by hyperextension and abnormal fixation of the legs on the thighs and flexion of the thighs on the abdomen. If this is seen, search should be made for other malformations.

It may be advisable to check with another film a day later, or after manipulation of the maternal abdomen, to see if the limbs change position.

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REFERENCES

1. BANKER, B. Q., VICTOR, M., AND ADAMS, R. D.: Arthrogryposis Multiplex Due to Congenital Muscular Dystrophy. *Brain* 80: 319-334, September 1957.
2. MEAD, N. G., LITHGOW, W. C., AND SWEENEY, H. J.: Arthrogryposis Multiplex Congenita. *J. Bone & Joint Surg.* 40-A: 1285-1309, December 1958.

SUMMARIO IN INTERLINGUA

Identification Radiographic de Congenite Arthrogryposis Multiplice in Utero

Congenite arthrogryposis multiplice pote a vices esser identificate in roentgenogrammas abdominal de ante parto per le constatation de hyperextension e fixation anormal del gambas super le femores e de flexion del femores super le abdomine. Es reportate duo casos de iste anormalitate in infantes neonate. In un revista del roentgenogrammas de ante parto, le condition es-

seva apparente in omne expositiones, ben que illo non haveva essite notate ante le parturition.

Congenite arthrogryposis multiplice es frequentemente accompagniate de congenite malformationes del cranio e del columna vertebral, de polydactylia, e de dislocation del coxa, e istos deberea esse cercate quando le diagnose es facite in utero.



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Stromal Endometriosis

A Case Report¹

JOSEPH M. WINSTON, M.D.,² and LUTHER W. BRADY, M.D.³

STROMAL ENDOMETRIOSIS is thought to be a primary uterine neoplasm arising from the stromal cell of the endometrium. It has been variously recorded as endometrial sarcoma, endometrial sarcoids, endolymphatic stromal myosis, stromal adenomyosis, proliferative stromatosis, perithelioma, fibromyosis, and endometrioma interstitiale (2-6). As far as can be determined, the first 2 cases were reported by Doran and Lockyer (1). Since then, about 100 cases have appeared in the English literature.

Hunter *et al.* (4) stressed the fact that the histologic structure tends to be the same whether the growth takes the form of uterine polyps or myoma-like masses, stating, also, that the histologic appearance does not furnish a true measure of the eventual outcome.

Stearns (6) states that while the disease is most often benign, it may be histologically malignant. It may invade normal tissue and metastasize to distant parts. The following case will serve to re-emphasize this entity.

CASE REPORT

S. B. H., a 42-year-old woman, was first seen at the Hospital of the University of Pennsylvania in May 1944, complaining of burning, pain, and frequency of urination following a course of x-ray therapy to the pelvis. In 1942 she had first noted severe right lower abdominal pain occurring during menstruation. Large blood clots were passed vaginally, and there was slight abdominal enlargement. Pelvic examination was reported to have revealed a large mass associated with the uterus, thought to be a fibroid. A supracervical hysterectomy was performed at another institution. On gross examination the uterus measured 10 × 12 × 14 cm., its cavity being distorted by a fibroid and filled with an overgrowth of firm yellow endometrium with hemorrhage on the free margins. The histo-

logic diagnosis was fibroma uteri with sarcomatous degeneration.

The patient did well until May 1944, when she experienced a recurrence of symptoms. Pelvic examination revealed a large mass with involvement of the lateral pelvic wall. An intravenous urogram failed to visualize the left kidney.

Since the lesion was thought to be malignant, it was decided to undertake a course of radiation therapy. The patient received a calculated dose of 3,450 rads (3,640 roentgens) to the midplane of the mass, through two anterior and two posterior portals, parallel and opposed, measuring 15 × 15 cm. each, with conventional voltage technic (200 kvp; 1.0 mm. Cu plus 1.0 mm. Al filtration; h.v.l. 1.0 mm. Cu), in thirty-seven elapsed days.

Physical examination at the time of her first follow-up visit, one month following completion of x-ray therapy, showed a stony hard mass occupying the greater portion of the true pelvis, more marked on the left. Three months later the mass was smaller but still prominent.

Interstitial implantation was then chosen as the modality of therapy. Eleven radium needles⁴ of 3.5 cm. active length, with 0.63 mg. of radium per centimeter, were implanted in the mass with uniform distribution. A calculated tumor dose of 4,200 rads was delivered in one hundred and sixty-eight hours.

Re-examination in January 1945 (four months following the implantation) revealed an excellent response along the medial portion of the mass but extension along the left lateral pelvic wall. Five radium needles of 3.0 cm. active length, with 0.5 mg. of radium per centimeter, and two radium needles of 5.0 cm. active length, with 0.5 mg. of radium per centimeter, were implanted in the mass and left in place for one hundred and twenty-one hours. The roentgenograms of the implantation showed an uneven distribution of the radium, making accurate calculation of dosage difficult. The dosage was estimated to be between 6,000 and 9,000 rads.

A pelvic examination in May 1945 revealed a residual mass along the left lateral pelvic wall. A calculated dose of 2,500 rads (2,650 roentgens) was delivered to the midplane of the mass through anterior and posterior parallel opposed portals measuring 15 × 15 cm., with conventional voltage technic

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⁴ All needles filtered with 0.5 mm. platinum.

(400 kvp; 2.0 mm. Cu plus 1.0 mm. Al filtration; h.v.l. 4.0 mm. Cu), in thirty-two elapsed days. There was prompt and satisfactory regression of the mass.

In March 1947, a mass was noted along the left lateral wall of the vagina. Ten radium needles of 5 cm. active length, with 0.5 mg. of radium per centimeter, were implanted in the mass, uniformly distributed in a 116-c.c. volume. The calculated dose was 3,500 rads delivered in one hundred and twenty hours. Gradual reduction in the size of the tumor mass occurred.

The patient was followed at six-month intervals and at each examination a mass was felt to the left of the vagina. There were no complaints referable to the pelvis, and further radiation therapy was not considered. In September 1957 sections from the 1942 hysterectomy were reviewed and showed the typical histologic appearance of stromal endometriosis, with islands of cellular tissue resembling endometrial stroma growing within smooth muscle of the myometrium. In several areas stromal tissue invaginated and invaded large endothelial-lined spaces, presumably lymphatics.

Eleven years after the last radium needle implantation, tenesmus developed, with the passage rectally of clear mucoid material containing blood. Associated with this was diminution in caliber of the stools. In December 1958 examination of the pelvis showed the rectum to be displaced to the right by a soft-tissue mass measuring 12 to 14 cm. in diameter. Barium-enema examination revealed a large extrinsic mass displacing and encroaching upon the rectum from the left side. The proctoscope could be inserted only 13 cm., when it encountered an extramucosal mass encroaching upon the lumen of the rectum but not invading the mucosa.

Since there had been rapid enlargement of the mass without demonstrable evidence of distant metastasis, exploration of the pelvis was performed. On opening the peritoneal cavity, a large cystic mass arising from the left pelvis was found. In removing the mass, the cavity was entered at its lowest portion and a considerable amount of bloody material evacuated. The greater part of the mass was removed, leaving a small portion deep in the pelvis attached to the left side of the rectum. There was no evidence of spread beyond the pelvis. The postoperative course was uneventful.

Gross examination of the specimen showed a cystic lesion approximately $5 \times 12 \times 14$ cm. There were areas in the cyst wall showing reddish brown friable tissue and others of yellow fat-like tissue.

Microscopic examination revealed in certain areas cells with plump, spindle-shaped nuclei and a moderate number of blood vessels, resembling compact endometrial strands with no glands. Mitotic figures were frequent. Other areas showed fibrous connective tissue intermingled with areas of smooth muscle. There was round-cell infiltration with

dilated cystic areas lined with cuboidal epithelium. Certain sections showed portions of a tube with rugae lined by ciliated columnar epithelium. The histologic examination of the tissues revealed endometrial stromatosis with post-irradiation fibrosis.

In July 1959 the patient again noted tenesmus and decrease in the caliber of the stools, associated with a left rectovaginal mass. In November 1959 a cystic mass containing blood was removed from the pelvis.

DISCUSSION

Stromal endometriosis occurs most frequently between the ages of thirty and fifty (6). The most common clinical symptoms are menometrorrhagia, dysmenorrhea, and pressure symptoms secondary to a pelvic mass. Other symptoms less frequently seen are leukorrhea, weight loss, and fatigue. Pelvic examination reveals an enlarged uterus, which may be symmetrical or irregular. Stromal endometriosis must be differentiated from endometriosis, uterine fibroids, and endometrial polyps.

At laparotomy the gross picture is characteristic. The uterus is enlarged, with multilobulated, rubbery tumors resembling myomata. The cut surface shows a typical turkish towel appearance, the projections retracting with great elasticity when stretched.

These tumors are generally localized to the uterus but may invade the bladder or bowel. They grow slowly and spread by the lymphatics locally (4). Distant metastases may occur *via* the vascular system, the most common site being the lung.

The treatment of choice for stromal endometriosis is a total hysterectomy with bilateral salpingo-oophorectomy, the operation being radical enough to remove all gross tumor (7). Bilateral salpingo-oophorectomy is recommended not only because of possible tumor spread, but also to remove the ovaries, which may promote growth of residual tumor.

Since it is difficult to ascertain the effects of radiation in stromal endometriosis, Symmonds *et al.* (7) suggest high-voltage roentgen therapy for all cases in which com-

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plete removal of the tumor is subject to question and in cases in which the neoplasm has recurred.

SUMMARY

1. Stromal endometriosis is a neoplasm of histologic innocence but unpredictable behavior. It is a rare lesion but a well established pathologic entity.

2. A case of stromal endometriosis has been presented with an eighteen-year follow-up.

3. The clinical signs and symptoms may be confused with uterine myomata. Familiarity with stromal endometriosis is necessary for correct therapy.

REFERENCES

1. DORAN, A. H. G., AND LOCKYER, C.: Two Cases of Uterine Fibroids Showing Peritheliomatous Changes: Long Immunity from Recurrence after Operation. *Proc. Roy. Soc. Med.*, London, 2: Section on Obst. & Gynec. 25-39, 1908-09.

2. GOODALL, J. R.: A Study of Endometriosis, Endosalpingiosis, Endocervicosis, and Peritoneo-Ovarian Sclerosis. Philadelphia, J. B. Lippincott Co., 1943.

3. HUNTER, W. C.: Benign and Malignant (Sarcoma) Stromal Endometriosis; Eleven-Year Progress Report of Previously Reported Cases; Ten New Examples, Including One Followed for Twenty-Four Years. *Surgery* 34:258-278, August 1953.

4. HUNTER, W. C., NOHLGREN, J. E., AND LANCEFIELD, S. M.: Stromal Endometriosis or Endometrial Sarcoma: A Reevaluation of Old and New Cases, with Especial Reference to Duration, Recurrences, and Metastases. *Am. J. Obst. & Gynec.* 72: 1072-1088, November 1956.

5. NOVAK, E.: Editorial Note *re* Stromal Endometriosis. *Obst. & Gynec. Survey* 12: 400-401, 1957.

6. STEARNS, H. C.: A Study of Stromal Endometriosis. *Am. J. Obst. & Gynec.* 75: 663-672, March 1958.

7. SYMMONDS, R. E., DOCKERTY, M. B., AND PRATT, J. H.: Sarcoma and Sarcoma-like Proliferations of the Endometrial Stroma. III. Stromal Hyperplasia and Stromatosis (Stromal Endometriosis). *Am. J. Obst. & Gynec.* 73: 1054-1070, May 1957.

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SUMMARIO IN INTERLINGUA

Endometriosis Stromal: Reporto de un Caso

Endometriosis stromal es de occurrentia rar, sed illo es un ben establite entitate. Es opiniate que illo es un primari neoplasma uterin que prende su origine in le cellula stromal del endometrio. Le condition debe esser differentiate ab endometriosis, fibroides uterin, e polypos endometrial. Illo es histologicamente benigne, sed su comportamento non es predicibile. Ben que usualmente confinate al utero, illo pote in-

vader le vesica o le intestinos, e metastases distante pote occurrer via le systema vascular, usualmente ad le pulmones.

Es reportate un caso que habeva essite sub observation durante dece-octo annos, con tractamento a intervallos per chirurgia, roentgeno-irradiation, e applicationes interstitial de radium. Le diagnose esseva verificata per le examine de un specimen chirurgic.



Vaginitis Emphysematosa¹

PAUL FRANCKE, JR., M.D.

VAGINITIS emphysematosa, or emphysematous colpitis, is characterized by multiple gas vacuoles in the subepithelial layers of the vaginal wall. In some cases the vaginal portion of the cervix is involved, resulting in a colpocervicitis emphysematosa. Less than 36 cases have been reported in English. Huguier (4) is credited with the first description of this condition in 1847. Ingraham and Hall, in 1934 (5), Bender and Jeffcoate in 1950

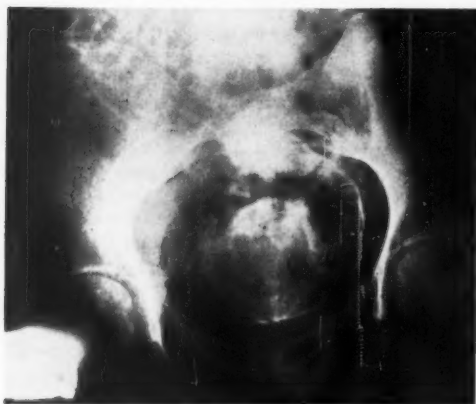


Fig. 1. Roentgenogram obtained Sept. 22, 1959. Numerous radiolucent spaces are readily visible in the pelvis. The ring-like soft tissue clouding in the center of the area is due to the dilated cervical lip, which is surrounded by carbon dioxide and air. Pelvic examination demonstrated the cervix to be dilated 5 cm.

(2), and Abell (1) in 1959, have reviewed the world literature.

Vaginitis emphysematosa occurs primarily in gravid patients, but has been found also in non-pregnant women. It produces few or no symptoms and clears within a short number of weeks following delivery. It is to be distinguished from gas gangrene of the uterus, which has a high mortality rate and is usually associated with abortion or cesarean section. X-rays have been useful in the diagnosis of this latter entity (6). The literature



Fig. 2. Lateral view, Sept. 22, showing the radiolucent areas to be between the rectum and bladder, conforming to the outline of the vagina.

yields no examples of roentgen diagnosis of vaginitis emphysematosa.

A 24-year-old colored primipara in labor, at term, required pelvimetry. Many ovoid radiolucent spaces from a few millimeters to 2 cm. in diameter were visible in the pelvis, located just anterior to the rectum, behind and under the fetal head, extending below the pubic symphysis. Physical examination demonstrated a boggy vaginal wall without gross evidence of infection. The mucosa presented a corrugated appearance. There was no instrumentation in the vagina prior to obtaining the original films. The patient had had a mild white vaginal discharge for years, which had been worse in the past three months. Diabetes was not present. The radiolucent spaces were still visible four days after delivery of a normal infant but their number was decreased. Nine weeks later they were absent. Cultures from the vagina demonstrated *Staphylococcus epidermis* and *Sarcinae*. Penicillin, however, had been administered twenty-four hours previously. No gas formation resulted from these bacteria. There was no growth under anaerobic conditions.

¹ Accepted for publication in January 1961.

The microscopic findings in the reported cases were more or less similar. Abell presents an excellent description. Empty ovoid cystic spaces throughout the substantia propria are the hallmark of this entity. No endothelial or epithelial lining could be demonstrated in the cystic lesions.



Fig. 3. Four days post partum (Sept. 26) the cystic spaces are still present. Note that they are visible at and below the pubic symphysis and the gas spaces, as a group, form a cone rather than a circular mass. This differentiates vaginitis emphysematosa from cystitis emphysematosa.

Accumulations of chronic inflammatory cells may be present about some of the cystic spaces, as well as in the submucosal areas.

Cystitis emphysematosa and pneumatosis cystoides intestinalis are two conditions with similar microscopic findings. These findings have also been produced experimentally by injecting gases into the subcutaneous tissues (7). Cystitis emphysematosa is known to be due to *Escherichia coli*, which produces carbon dioxide.

The nature of the gas in vaginitis emphysematosa has remained a mystery until recently. It has been found to be carbon dioxide (3). Up to the present, no organism has been linked to this entity, but *Escherichia coli* is probably the one involved.



Fig. 4. Barium in the vagina demonstrating the indentations of gas cysts in the wall, producing the corrugated appearance seen on direct inspection (Oct. 3, 1959).

Cystitis emphysematosa, pneumatosis cystoides intestinalis, fat-containing tumors of the pelvis, gangrene, gas in the bowel, and a tampon in the vagina must all be considered in the differential radiological diagnosis.

SUMMARY

Vaginitis emphysematosa, or gas formation in the vaginal wall, may be added to the list of diseases that can be diagnosed radiologically.

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REFERENCES

1. ABELL, M. R.: Cervicocolpitis (Vaginitis) Emphysematosa. *Surg., Gynec. & Obst.* **107**: 631-638, November 1958.
2. BENDER, S., AND JEFFCOATE, T. N. A.: Vaginitis Emphysematosa. *J. Obst. & Gynaec. Brit. Emp.* **57**: 432-436, June 1950.
3. HOFFMAN, D. B., AND GRUNDFEST, P.: Vaginitis Emphysematosa; a Case Report. *Am. J. Obst. & Gynec.* **78**: 428-430, August 1959.
4. HUGUIER, P. C.: Mémoire sur les kystes de la matrice et sur les kystes folliculaires du vagin. *Mém. Soc. chir., Paris* **1**: 241-376, 1847.
5. INGRAHAM, C. B., AND HALL, I. C.: Emphysematous Vaginitis. *Am. J. Obst. & Gynec.* **28**: 772-782, November 1934.
6. POPPEL, M. H., AND SILVERMAN, M.: Gas Gangrene of the Uterus. *Radiology* **37**: 491-492, October 1941.
7. WRIGHT, A. W.: The Local Effect of the Injection of Gases into Subcutaneous Tissues. *Am. J. Path.* **6**: 87-124, March 1930. Cited by Abell (1).

(Pro le summario in interlingua, vider le pagina sequente)

SUMMARIO IN INTERLINGUA

Vaginitis Emphysematose

Vaginitis emphysematose, i.e. formation de gas in le pariete vaginal, debe esser addite al lista del morbos que pote esser diagnosticate roentgenologicamente.

In le curso del pelvimetria in un femina negre in labores, esseva demonstrate in le pelve le presentia de numerose ovoide areas radioluciente, de diametros de inter pauc millimetros e 2 cm, justo anterior al recto, al retro e in basso del capite fetal, e exten-

dente se infra le symphyse pubic. Quatro dies post le parturition, le numero de iste areas habeva declinate, e novem septimanas plus tarde il esseva trovate que illos habeva disparite.

Vaginitis emphysematose debe esser distinguite ab cystitis emphysematose, ab pneumatosis intestinal, ab tumores pelvie a contento grassiose, e ab le presentia de un tampon in le vagina.



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Low Temperature Barium-Water Suspensions for Roentgenologic Examination of the Colon¹

GEORGE LEVENE, M.D.

IT HAS long been common practice to administer barium enemas at "comfortable body temperature." Hot or cold water is added until the suspension is "comfortably warm" on the more sensitive skin of the volar aspect of the forearm, the temperature usually varying from 100 to 110° F. For a number of years it has been our practice to use water at 41° F. In our geographic climate this is obtained from the cold water faucet in winter and at other times the water is chilled to this temperature. After use in several thousand cases, this method has proved to possess certain advantages.

One of the difficulties frequently encountered in examining the colon by enema is the inability of the patient to retain the barium suspension. It is common practice, therefore, to insert a balloon into the rectum and inflate it so that the lumen is occluded. Since the balloon completely obscures the rectum, and since 30 per cent of all gastrointestinal cancers occur in this portion of the bowel (1), it is obvious that such a practice definitely militates against detection of a most serious possible lesion.

It is well known that hyperemia of the colon produces irritability. Such irritability is seen in inflammatory lesions of the colon, ulcerative colitis, tuberculosis of the cecum (Stierlin's sign), and chemical or drug irritation. Water at a temperature of 110° F. may be comfortable to the skin on the forearm, but in the colon it produces active hyperemia. While the colon itself lacks thermal sensitivity, it responds to the effect of heat transmitted through its wall to the blood vessels which penetrate it. Cold, on the other hand, results in local ischemia, and, depending on the temperature and its duration, produces a variable degree of anesthesia in any body area with which it is in contact. A cold suspension

of barium sulfate is therefore conducive to more complete and more comfortable retention in the colon.

It has been shown that "application of warmth to the region of the anus causes reflex relaxation of the (anal) sphincter; application of cold increases its tonic contraction." The contracted anal sphincters assist the patient in retaining the enema. Moreover, according to the law of reciprocal innervation, "stimuli in the colon or rectum which give rise to a defecation reflex cause a reciprocal contraction of the lower bowel and relaxation of the anal sphincters. Conversely, stimulation (contraction) of the anal canal leads to reflex dilatation of the bowel" (2). By virtue of this physiologic mechanism cold suspensions of barium are more easily instilled into the relaxed colon and are more easily retained with the help of the contracted sphincters.

Double-contrast examination of the colon is usually employed for the detection of polyps. Air has always been used as the second contrast medium (3, 4), although compressed carbon dioxide has been shown to be far superior for the purpose (5, 6). Radiologists are aware of the annoying bubbles which confuse the identification of polyps. Since all gases—air, as well as carbon dioxide—are more soluble in cold than in warm solutions (7), the formation of these annoying bubbles is minimized when the barium suspended is of a lower temperature.

CONCLUSIONS

Barium suspensions for roentgenologic examination of the colon prepared at a much lower temperature than commonly employed possess many advantages:

1. Less hyperemia and therefore less irritability are produced.

¹ From the Department of Radiology, Boston University-Massachusetts Memorial Hospitals Medical Center, Boston, Mass. Accepted for publication in January 1961.

2. The mild anesthetic effect of the colder suspension raises the threshold of excitability. This results in better and more comfortable retention of the enema.

3. Tonic contraction of the anal sphincters is stimulated, contributing to the ease of retention.

4. Relaxation of the colon, in accordance with the law of reciprocal innervation, permits more rapid flow of the enema with less tenesmus and discomfort to the patient.

5. There is reduction of the tendency to bubble formation of the air or carbon dioxide used in double-contrast examinations, since all gases are more soluble in cold than in warm liquids.

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REFERENCES

1. MCKITTRICK, L. S.: *Cancer. A Manual for Practitioners*. Boston, Massachusetts M. Soc., 1940.
2. STARLING, E. H.: *Principles of Human Physiology*. Revised by C. L. Evans. Philadelphia, Lea & Febiger, 1933, 6th ed.
3. SHAY, H., AND GERSHON-COHEN, J.: The Diagnostic Value of Double Contrast Enema, with Special Reference to the Diagnosis of Early Neoplastic Lesions of Colon. *Surg., Gynec. & Obst.* **58**: 52-57, January 1934.
4. BOLES, R. S., AND GERSHON-COHEN, J.: Intestinal Tuberculosis. Pathologic and Roentgenologic Observations. *J.A.M.A.* **103**: 1841-1845, Dec. 15, 1934.
5. LEVENE, G., AND KAUFMAN, S. A.: An Improved Technic for Double Contrast Examination of the Colon by the Use of Compressed Carbon Dioxide. *Radiology* **68**: 83-85, January 1957.
6. LEVENE, G.: Rates of Venous Absorption of Carbon Dioxide and Air Used in Double-Contrast Examination of the Colon. *Radiology* **69**: 571-573, October 1957.
7. HAMILL, W. H., AND WILLIAMS, R. R., JR.: *Principles of Physical Chemistry*. Englewood Cliffs, N. J., Prentice-Hall, Inc., 1959.

SUMMARIO IN INTERLINGUA

Suspensiones de Barium in Aqua a Basse Temperaturas pro le Examine Roentgenologic del Colon

Suspensiones de barium pro le examine roentgenologic del colon, preparate a 41 F plus tosto que al communmente usate temperatura "confortabile" del corpore, ha multe advantages:

1. Es producite minus hyperemia e ergo minus irritabilitate.

2. Le levemente anesthetic effecto del reducite temperatura del suspension leva le limine de excitabilitate. Isto resulta in un meliorate e plus confortabile retention del clyster.

3. Le contraction tonic del sphincteres

anal es stimulate, e assi le retention es rendite plus facile.

4. Le relaxation del colon, causate secundulo le lege del innervation reciproc, permette un plus rapide fluxo del clyster, con minus tenesmo e minus discomforto.

5. Il occurre un reduction del tendentia del formation de bullas de aere o del bioxydo de carbon que es usate in examines a duple contrasto, proque omne gases es plus soluble in liquidos frigide que in liquidos calide.

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Legislative Aspects of Radiation¹

CAREY BREWER, Ph.D.²

AS A STAFF representative of the Joint Committee on Atomic Energy, it is a privilege for me to discuss some of the legislative aspects of radiation. While I am not in a position to give a complete run-down of legislative proposals relating to radiation which the Congress may consider in the session beginning in January, I can review the general nature of legislative concern in this field and mention some of the recent activities of the Joint Committee and its staff which may be of interest.

Since its inception, fourteen years ago, the Joint Committee has been concerned with radiation matters. A fundamental problem facing the people of the United States, and thus their elected representatives in Congress, has been how to reap the manifold benefits of atomic energy and ionizing radiation without incurring unacceptable hazards to the public health and safety. In attempting to deal with this phase, the Committee has enjoyed the counsel and assistance of many distinguished members of the Radiological Society of North America.

The legislative aspects of radiation consist mainly of those steps taken by the Congress to promote safety, both in the use of radiation and in the operation of atomic energy programs which pose a potential radiation hazard. These include legislative enactments affecting the licensing and regulatory functions of the U. S. Atomic Energy Commission as well as the setting of radiation protection standards throughout the Federal Government.

Congressional actions aimed at development of economic atomic power and increased uses of radioisotopes in industry, medicine, and agriculture, may be termed legislative aspects of radiation, in a positive sense.

In the first category, regulation, the legislative concern is to protect the health and safety of our people, while in the second it is to promote the beneficial uses of radiation. In both areas, the terms of the Atomic Energy Act, as amended in 1954, are quite broad, permitting flexibility in the administration of the program.

EXECUTIVE AGENCY ACTIVITIES

Administrative responsibilities in the field of radiation protection are spread throughout the Federal Government. The regulatory functions of the Atomic Energy Commission have to do mainly with the task of ensuring that all phases of the atomic energy program are operated in compliance with standards designed to protect the health and safety of the public, including workers in the atomic energy industry. Some dozen other Federal agencies are also concerned with radiation protection. Those having major responsibilities include the Public Health Service, the Food and Drug Administration, and the Departments of Defense, Labor, and Commerce.

As an overall coordinating body, the Federal Radiation Council was established in 1959 first by Executive Order and later by statute to "advise the President with respect to radiation matters, directly or indirectly affecting health, including guidance for all federal agencies in the formulation of radiation standards and in the establishment and execution of programs of cooperation with States..." The Council currently consists of the heads of the five Federal agencies most directly concerned with the problems of exposure to radiation—the Department of Health, Education and Welfare, the Atomic Energy Commission, and the Departments of Defense, Labor, and Commerce. The

¹ Presented at the Forty-sixth Annual Meeting of the Radiological Society of North America, Cincinnati, Ohio, Dec. 4-9, 1960.

² Professional Staff Member, Joint Committee on Atomic Energy.

AEC, as well as all other Federal agencies, is subject to "guides" prescribed by the Council.

Finally, AEC activities must be closely coordinated with those of State and local governments, which have long had the responsibility of protecting their citizens from the hazards of many radiation sources, including x-ray machines and naturally radioactive elements such as radium. In addition, under Public Law 86-373 of 1959, regulatory responsibility over certain radiation sources—principally radioisotopes—may be gradually transferred, under prescribed safeguards and conditions, from the AEC to State governments.

In this connection, the Joint Committee staff is currently making a study of the AEC regulatory process, including alternatives for different forms of organization to license and regulate nuclear materials and facilities. This work will be completed early in the next session of Congress and may serve as a basis for revision of the regulatory procedures or organization of the AEC.

ACTIVITIES OF THE JOINT COMMITTEE

While the Joint Committee on Atomic Energy has been concerned with the entire range of radiation matters, particular emphasis has been given to safety. In recent years the Committee has conducted extensive hearings and investigations in those areas of the atomic energy program which pose especially serious hazards to the public. In 1957 the Committee established the Special Subcommittee on Radiation, because of its intense concern with this problem. Under the chairmanship of Congressman Chet Holifield, this Subcommittee has conducted hearings and issued summary-analysis reports on fall-out (1957 and 1959), radioactive waste disposal (1959), the biological and environmental effects of nuclear war (1959), and the basis and use of radiation protection standards (1960).

The Joint Committee's Subcommittee on Research and Development has examined at length the problems of employee radia-

tion hazards and workmen's compensation. Over the years the Committee has also devoted considerable attention to other aspects of radiation, such as food irradiation and isotope development.

HEARINGS ON RADIATION PROTECTION STANDARDS

Probably of greatest interest to radiologists are the hearings of the Special Radiation Subcommittee on radiation protection standards which were held this past spring and were recently issued in printed form, together with a summary-analysis report (1). The purpose of the hearings was to examine the basis and use of radiation protection standards. We were concerned not only with the origin or source of the standards in current use, but also with the underlying concepts. Of prime interest to the Subcommittee was the role being performed by the Federal Radiation Council, whose organic law had been drafted and approved by the Joint Committee preliminary to Congressional passage in 1959.

Also of interest to the Subcommittee were the respective roles of the National Committee on Radiation Protection and Measurements (NCRP) and the International Commission on Radiological Protection (ICRP), whose recommendations have had a substantial influence on Federal policy in radiation protection.

While the NCRP and the ICRP are non-governmental, their recommendations have formed the backbone of Federal regulations setting forth basic standards of radiation protection. The specific figures embodied in NCRP-ICRP recommendations concerning radiation exposure limits have been incorporated into Federal rules and regulations governing the operation of the entire atomic energy program.

Witnesses presenting testimony at the Subcommittee hearings were in full agreement as to the outstanding contribution which the NCRP and the ICRP have made in the formulation of radiation standards. A question was raised, however, as to whether the Government is properly discharging its responsibility or whether it is

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IMPLICATIONS OF STANDARDS

The importance of the foregoing question—and, indeed, the importance of establishing valid standards—were underscored at the hearings by testimony setting forth two basic facts:

1. The use of atomic energy and other sources of ionizing radiation is inevitably accompanied by the exposure of some persons to man-made ionizing radiation.

2. The most reasonable working assumption for protection purposes is that all such exposures, however small, have an associated biological risk.

Given these facts (the exposure of persons and the consequent risk of harmful biological effects), it follows that the setting of standards to *limit* radiation exposures to specified levels involves the exercise of basic value judgments. How does one determine the degree of risk which atomic energy workers should accept? Who should decide on the biological risk to which the whole population should be exposed? Are these functions which might properly be performed by essentially private associations, such as the NCRP and the ICRP?

The far-reaching implications of these questions become readily apparent when one considers the economic aspects of radiation protection standards. Extremely stringent standards of exposure, for example, could increase substantially the cost of shielding an atomic reactor or the cost of handling and using radiation source materials. To the extent that radiation protection costs significantly increase the overall cost of nuclear projects, there is a possibility that some projects might be priced out of the market. On the other hand, if the standards are not sufficiently stringent, the exposure to workers and surrounding populations could be unacceptable.

The essential point to be considered is not whether the NCRP and the ICRP have produced valuable and useful recommen-

dations, but rather how these recommendations should be applied to public policy decisions.

ROLE OF THE FEDERAL RADIATION COUNCIL

The creation of the Federal Radiation Council in 1959 had been interpreted by some as meaning that it would make the basic policy decisions respecting the establishment of radiation protection standards. It was anticipated that the Council would bring into consideration relevant social and economic factors in formulating standards to be applied by all agencies of the Federal Government in this field.

Testimony presented at the Subcommittee hearings and the actions of the Federal Radiation Council to date, however, indicate that the Council is not performing such a role. Thus far, the individual Federal agencies developing and promulgating radiation protection standards apparently have been little affected by the Council. Its one memorandum issued since its creation essentially endorses the standards already being used and provides for the use of somewhat changed terminology. The memorandum itself is considered a "guide," not a binding directive which must be adhered to by all Federal agencies.

In brief, the Council memorandum, which was approved by the President and published in the Federal Register, sets forth seven recommendations for the guidance of Federal agencies. These include a table of numbers and the new terms "radiation protection guide" and "radioactivity concentration guide" to be used in place of "maximum permissible dose" and "maximum permissible concentration," which terms were said to have unfortunate connotations not intended by the NCRP and the ICRP.

The final recommendation of the guide admonishes the agencies to "... apply these Radiation Protection Guides with judgment and discretion, to assure that reasonable probability is achieved in the attainment of the desired goal of protecting man

from the undesirable effects of radiation." This is followed by a notation that "the Guides may be exceeded only after the Federal agency having jurisdiction over the matter has carefully considered the reason for doing so in light of the recommendations in this paper."

It should be noted that the memorandum indicated that the Council intended to follow the activities of Federal agencies in an effort to promote coordination. In fact, two months after issuing the memorandum, the Chairman of the Council formally requested fourteen agency heads to report on their activities falling within its scope. Several weeks later he advised the President that the agencies were complying with the guide-lines set forth in the memorandum.

Whatever view one takes with respect to the need for central direction and control of Federal agency activities in radiation matters, it is evident that the Federal Radiation Council thus far has been a loose coordinative device. Several members of the Joint Committee have questioned whether the Council is carrying out the functions originally intended for it, particularly with respect to the policing of other agencies to ensure compliance with the basic objectives of Federal policy in this field.

Some of the specific questions raised are these:

1. Where does final responsibility reside for the imposition of standards embodied in Agency regulations affecting the economic and social welfare of the public? Is the Federal Radiation Council, the President, or each individual agency responsible?

2. Must the standards applied by individual Federal agencies be justified in accordance with established administrative procedures within the agencies, or does the Federal Radiation Council memorandum, which was issued as a Presidential directive, remove conventional requirements of this type?

3. To what extent has the Federal Radiation Council relieved the individual agencies of responsibility in making judg-

ments of overall economic and social import?

4. If a number of individual agencies are authorized to set standards of radiation exposure within the confines of permissible limits or "radioactivity concentration guides," for general population exposure, who allocates quotas to ensure that the total does not exceed the established limits? Is each agency free to pre-empt the full limits of exposure in the entire pool in pursuing its own objectives? Should not each significant additional contribution be reviewed by the FRC in order to consider each incremental contribution in relation to the whole?

In view of these unsettled questions, perhaps some members of the Joint Committee may wish to consider in the next session legislation designed to provide a mechanism of stronger central direction and control than that represented by the Council. In this connection, Subcommittee Chairman Holifield recently stated his view that "the pressing need in the field of radiation protection is to establish appropriate Federal machinery for broad policy decisions that must be made." He further observed that, "if the Federal Radiation Council cannot be modified to perform this function, or if it is unwilling to do so, then the remedy may lie in replacing the FRC with a different type of Federal Agency" (2).

FUTURE OF THE NCRP

Assuming that the Federal Radiation Council will perform its intended function in the future, an important remaining question concerns the future role of the National Committee on Radiation Protection. Will the existence of an official agency charged with responsibility in the standards-setting field eliminate the need for such an independent group?

At the Subcommittee hearings it was noted that the NCRP not only furnished the basic data and specific recommendations on which the Federal Radiation Council guide is based, but that its membership was called upon to do much of the

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staff work in formulating the guide. It was also indicated that some of the members of the NCRP are Government employees who might be placed in a difficult position if their views as NCRP members should be in conflict with the policies set forth by the FRC.

Witnesses testifying at the hearings strongly supported the view that the NCRP should persist in its traditional functions of scientific study and evaluation of technical data and that no bar should be placed in the way of continued participation by Government employees in the work of the NCRP.

Significantly, the Chairman of the Federal Radiation Council as well as members of the Subcommittee expressed agreement with this view.

The fundamental difference between the role of the NCRP and that of the Federal Radiation Council has been emphasized by Subcommittee Chairman Holifield. In a recent address he drew a distinction between the task of scientific inquiry and the formulation of public policy, stating his view as follows:

"There is a significant continuing role to be performed by groups such as the NCRP and its international counterpart, the International Commission on Radiological Protection (ICRP). There will always be a need for independent collection and examination of scientific data. Moreover, independent analysis of problems and appraisals of alternative courses of action, as well as criticism of public policy, will always contribute heavily to the advancement of protection in this field and will tend to ensure responsible governmental action. But the final judgments going into the make-up and application of standards as public policy must be made by government" (2).

From the testimony presented at the hearings there is every indication that the NCRP will continue to perform a valuable service in the radiation protection field.

Finally, with respect to the legislative aspects of radiation, certain observations can be stated. Legislation in this field

must of necessity be general in nature. Congress can set forth broad objectives in the form of legislation, but the details must be worked out by the Atomic Energy Commission and other administrative agencies with the technical advice which organizations such as the national radiological societies and the NCRP can render.

Any substantial changes which Congress might make are likely to be in the realm of organization or procedural matters. For example, the organization or the Atomic Energy Commission or the Federal Radiation Council could be modified by statute, or Congress might legislate on the role of public hearings or the functions of the Advisory Committee on Reactor Safeguards, but legislation would not extend to the setting of detailed radiation standards.

Congress and the Joint Committee on Atomic Energy, as well as the Atomic Energy Commission, will continue to need expert advice and technical assistance in the field of radiation. To quote Congressman Holifield once again: "...improved Federal organization is not the sole answer to the various problems and issues of radiation exposure which have been accentuated by our burgeoning nuclear technology. The development and refinement of new concepts in radiation protection and the accumulation of new scientific data are functions residing with the scientific community at large, and in the long run these functions will influence decisively the functions performed by government at all levels."

Joint Committee on Atomic Energy
Congress of the United States
Washington, D. C.

REFERENCES

1. Radiation Protection Criteria and Standards: Their Basis and Use. Hearings before the Special Subcommittee on Radiation of the Joint Committee on Atomic Energy, Congress of the United States, 86th Congress, 2d Session, May 24-26 and May 31-June 3, 1960. Summary-Analysis, October 1960.
2. HOLIFIELD, C.: Address of Congressman Chet Holifield, Chairman of the Special Radiation Subcommittee of the Joint Committee on Atomic Energy, Presented at the Fifth Annual Meeting of the Health Physics Society, Boston, Mass., June 30, 1960.

SUMMARIO IN INTERLINGUA
Aspectos Legislative del Radiation

Depost su inception dece-quatro annos retro, le Committee Juncte pro Energia Atomic es concernite con le radiation. Illo ha sublineate particularmente le factor del securitate, e in 1957 illo establiva un Subcommittee Special pro Radiation. Le responsabilitates administrative in le campo del protection contra le radiation es distribuite a transverso le brancas del governmento federal, e le Consilio Federal pro Radiation, establite in 1959, age como un corpore de coordination general. Testificationes esseva recipite per le Subcommittee Special pro Radiation in le primavera de 1960 con le objectivo de examinar le base e le uso de standards de protection contra le radiation, con referentias special al rolo del Consilio Federal pro Radiation e al rolos respective del Committee National pro le Protection e Mesuration Radiatori (NCRP) e del Commission International pro le Protection Radiologic (ICRP).

Esseva notate un consenso complete quanto al eminente contributiones facite per le NCRP e le ICRP in le formulation de standards de radiation, sed le question esseva sublevate si le governmento satisfacadequatemente su responsabilitate o si illo accepta troppo extensamente le recommendationes de gruppos private. In plus, le NCRP e le ICRP ha formulate importante e utile proponimentos, e le question de lor application a decisiones con respecto a politicas public debe esser solvite.

Le testantes supportava energicamente le conception que le NCRP debe persiste in su functiones traditional de studio scientific e de evaluation de datos technic.

Le legislation in iste campo debe necessariamente esser de natura general. Omne considerable modification que le Congresso pote introducir va esser sin dubita in le area de organisation e del aspectos procedimental.



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WORK IN PROGRESS

Chemical Protection Against X-Radiation in the Guinea-Pig¹RICHARD WAGNER, M.D., and
IRVING B. JOFFE, M.D.

Chapman, Sipe, Eltzholtz, Cronkite, and Chambers (1) first demonstrated the beneficial effect of glutathione injection on the x-ray induced mortality rate and weight loss in mice. We found the same effect in guinea-pigs of 200 to 300 gm. body weight on exposure to 200 to 250 r. Each animal was injected with 100 mg. glutathione immediately before and after irradiation.

Glutathione concentration ranges in normal guinea-pigs from 100 to 140 mg. per 100 ml. erythrocytes, with only approximately 8 to 10 per cent loss of stability, following incubation with acetylphenyl hydrazine. In irradiated nonprotected controls, the glutathione concentration reaches extremely low levels, and the glutathione loses its stability (approximately 50 per cent and more), while there is a considerable depression of the leukocytes in the peripheral blood. In the irradiated and protected animals the glutathione erythrocyte levels were found to be considerably higher, though there is likewise some loss of stability.

Glutathione stability depends on reduced triphosphopyridine nucleotide (TPN); therefore, glucose 6-phosphate dehydrogenase and 6-phosphogluconic dehydrogenase activity were also studied in preliminary experiments to investigate the loss of stability. This is measured by the difference in optical density per gram of hemoglobin per minute. In the nonprotected group it was lower than in the protected; the lowest value in the former was 4.02, the highest in the latter 11.9.

Most striking results were recently obtained in a small series of experiments with protection due to injection of the sodium salt of ribonucleic acid. Nine guinea-pigs were irradiated with 250 r (LD 50 dose 200 r) and injected with 100 mg. sodium ribonucleate before and after irradiation; 9 animals without protection by ribonucleic acid served

as controls. Seven of the nonprotected animals died within ten to twenty-seven days following irradiation, while only 3 of the protected animals died ten days after irradiation, one of them, however, on the third day. This fatality cannot be attributed to radiation damage. The survivors were still alive forty days after irradiation and in perfect condition.

The 2 survivors were re-irradiated with 275r, and 6 of them were again protected with 100 mg. sodium ribonucleate before and after irradiation. The 2 nonprotected guinea-pigs died twelve days after irradiation; 4 of the protected animals were still in perfect condition after four weeks.

At the present time experiments are in progress, using a low-molecular-weight ribonucleic acid, prepared from yeast according to Monier *et al.* (2). This will be studied in normal guinea-pigs as well as in tumor-bearing mice.

It is possible that the depression of the glutathione level in the erythrocytes might be accompanied by simultaneous increase of sulfhydryl-containing precursors, such as L-cysteine or L-glutamylcysteine.

REFERENCES

1. CHAPMAN, W. H., SIPE, C. R., ELTZHOLTZ, D. C., CRONKITE, E. P., AND CHAMBERS, F. W., JR.: Sulfhydryl-Containing Agents and the Effects of Ionizing Radiations. 1. Beneficial Effect of Glutathione Injection on X-Ray Induced Mortality Rate and Weight Loss in Mice. *Radiology* 55: 865-873, December 1950.
2. MONIER, R., STEPHENSON, M. L., AND ZAMECNIK, P. C.: The Preparation and Some Properties of a Low Molecular Weight Ribonucleic Acid from Baker's Yeast. *Biochim. et biophys. acta* 43: 1-8, Sept. 9, 1960.

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¹ From the Research Laboratory of The Boston Floating Hospital, the Department of Pediatrics, Tufts University School of Medicine, and the Department of Radiology, Boston Dispensary, Boston, Mass.

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EDITORIAL

From a Purely Radiological Point of View

*Shadows are but dark holes in radiant streams, twisted rifts
beyond the substance, meaningless in themselves.*

*Man—warm, lively, fleshy man—and his story are both root
and key to his shadows; shadows cold, silent, and empty.*

JOHN CAFFEY

The bold, brave, boyishly boastful slogan of the United States Army Corps of Engineers, "The difficult we do immediately—the impossible takes a little longer," may well apply to diagnostic radiologists. From visual clues often barely perceptible they extract knowledge that is safe, sound, significant, and satisfying much of the time. Pathologists, fellow students of organs altered by disease, do not regularly risk their reputations with reports resting on gross morbid changes alone, even though their pieces of evidence are polychromatic and substantial, and can be felt, smelled, weighed, and cut or caressed with a knife. What is the secret of drawing valid conclusions from shadow to substance with a frequency that is astonishing and delightful?

The secret is simple though not altogether conscious; roentgen cues, like those used in crime detection, are not weighed *in vacuo*. Roentgenograms belong to patients and each patient has a story: age, sex (recently complicated by finesses found in the sex chromosome pattern), a health record past and recent, and a constellation of findings, the "clinical picture" or "clinical problem." When interpreting roentgenograms, what we see we judge in the light of what we know. Generalized loss of bone mineral (to borrow an example) may suggest hyperparathyroidism in a patient with recurrent kidney stones, deficiency of vitamin D and calcium ("osteomalacia") if associated with chronic small-bowel disease, postmenopausal osteoporosis in a woman past her second age of

blushing, or multiple myeloma if found in an elderly patient with bone pain, loss of strength, anemia, and proteinuria. Roentgen signs, like other signs in medicine, in nature, art, or human language, gain their meaning from their context.

One misapprehension spread, if not sanctified, by custom deserves to be mentioned in order to be dispelled. Some doctors requesting radiologic consultation like to withhold important knowledge about their patient in order to avoid "influencing" the radiologist, even though this is not customary with other consultants. A few of us—a very few among the very best—like to look at films before they know the problem at hand. For the sake of their sanity, diagnostic radiologists must develop a taste for puzzles, and a jigsaw puzzle can be more absorbing if some of the pieces are missing. As an intellectual exercise properly practiced at meetings of radiologists, it can be entertaining and educational to consider films in isolation; suggesting the correct diagnosis on sparse evidence gives one great satisfaction. But in everyday life it is not edifying to look at roentgenograms with no knowledge of the individual whose organs were examined or the ills that sent him to the doctor. Obtaining a proper clinical history is usually the most rewarding step in the diagnostic process; at the bedside, questioning the patient about his complaints past and recent precedes physical examination. No one is concerned that the eyes and ears and palpating fingers of surgeons and internists will betray them

because they know their patient and their minds are not empty of ideas about what could make him sick. Are radiologists less to be trusted?

There is no conflict between a diagnostic radiologist's need for knowing his patients and his need for an independent mind in looking at films, assuming what must be assumed, intellectual honesty. As an internist is not misled by the clinical history into finding an enlarged liver or spleen where there is none, a radiologist will not consider a heart abnormal in size or shape merely because he knows that the patient has suggestive symptoms or a significant murmur. Otherwise one would often land in a situation not unlike that of the weather man who amended a "Continuing fair and mild" forecast to "Fair and mild with a chance of light showers" when he noticed from his office window that the streets below were wet; he did not realize that the water came from a water cart. Abnormalities are not *found* because of a given clinical history, but they are *judged* in the light of it. A boot-shaped heart and small pulmonary vessels in a cyanotic infant are diagnostic of Fallot's tetrad if the electrocardiogram shows right ventricular hypertrophy; identical roentgen findings in a cyanotic infant with left ventricular hypertrophy are almost conclusive evidence for atresia of the tricuspid valve. A heart of normal size is not ordinarily an exciting observation, but in a patient with severe pulmonary emphysema it may indicate generalized cardiac dilatation from a decompensated cor pulmonale. In a child with pulmonary emphysema caused by mucoviscidosis a normal-sized heart may be ominous since it is often the sign of terminal heart failure.

It might be objected that films are a radiologist's proper domain and that he should avoid using additional information in interpreting them, but even if this were desirable it could not be accomplished. The mere fact that a patient was examined in a given office or at a certain hospital, the time of the day and the time of the year, his age, development, degree of nu-

trition, all apparent on roentgenograms—all these furnish important secondary clues; sex, as elsewhere, may play an important role. A defect in the sigmoid colon of a patient examined because of blood in the stools will suggest one disease if the patient is elderly and emaciated and another in a woman in the menstruating age; radiographically, carcinoma of the colon and endometriosis of the colon can be remarkably alike. Detailed clinical information is not always available to the radiologist and from the roentgenogram alone he can correctly guess much about a patient, but for an intelligent opinion in a diagnostic problem case he has to learn the rest from the patient, from his chart, from his other doctor (1). The question is not *whether* a diagnostic radiologist needs clinical information to interpret his films properly, but *how much* additional information he needs in the best interest of his patient.

What makes diagnostic radiology interesting is that it is part of medicine; examining metal castings would be less absorbing than examining patients. What makes it difficult is that it encompasses all medicine. A good radiologist is a good doctor who knows much about disease and the ways it affects people, their tissues, their organs, and their functions. It is in the interest of his patients that he puts to use all of his knowledge of clinical medicine when he examines them and does not merely rely on remembered patterns of morbid black and white images. Radiologists like other doctors learn medicine at the bedside; patients, not pictures, are their source of knowledge, and they see many patients, more than most of their colleagues. Moved by the proper spirit they could put this experience to use to enlarge the scope of their specialty, helping diagnostic radiology evolve into *the specialty of medical diagnosis* (1).

STEVEN E. ROSS, M.D.
San Francisco, Calif.

REFERENCE

1. Ross, S. E.: The Role of the Radiologist in Medical Diagnosis. Editorial. J.A.M.A. 174: 2224-2225, Dec. 31, 1960.

IN MEMORIAM



SAMUEL W. DONALDSON, M.D.

1891-1961

Society, the medical profession, and radiology in particular have suffered a severe loss in the death on April 10, 1961, of Dr. Samuel W. Donaldson at his home in Ann Arbor, Mich.

Doctor Donaldson ("Sam," as he was known to most of us) held a unique position in radiology in the United States and Canada. Through his position as Director of the Professional Bureau of the American College of Radiology for many years, he became

well known to the officers of the College, the officers of both the American Roentgen Ray Society and the Radiological Society of North America, and to the members of both organizations. His place will be hard to fill. His ready smile, genial nature, and ready wit made him a favorite with everyone.

Doctor Donaldson was born in Rockford, Tenn., on Sept. 14, 1891, and received his early education in Asheville, N. C., and Knoxville, Tenn., graduating

from Knoxville High School in 1907. He spent one semester in the University of Alabama and then entered the University of Tennessee, where he was granted his Bachelor of Arts degree in 1912. He received his M.D. from the University of Michigan in 1916 and interned at Lenox Hill Hospital in New York City. He served as an officer in World War I and was discharged as a Major.

Dr. Donaldson's early training in radiology was at the University of Michigan, where he was an instructor in Radiology from 1921 to 1923. He established the Department of Radiology at St. Joseph's Hospital in Ann Arbor in 1923 and remained in practice there until his death. He became radiologist to Ypsilanti State Hospital at Ypsilanti, Mich., in 1946. He was current Chairman of the Medical-Legal Committee of the Radiological Society of North America and Second Vice-President of the American Roentgen Ray Society. He had a special

flair for statistics and contributed to the knowledge of the economics of radiological practice both by publication and by committee reports.

Dr. Donaldson married Kathryn P. Overman in 1919 in Danville, Ill. She died in 1954 and in 1957 he married Margaret L. Lowe of Seattle, Wash., who survives him. Surviving also are a son, John G. of Madison, Wisc., and a daughter, Mrs. G. B. (Mary E.) Hotchkiss of Washington, D. C.

The Board of Chancellors in February 1956, awarded Doctor Donaldson the Gold Medal of the American College of Radiology. This was ample proof of the high esteem in which he was held and a fitting acknowledgment of his contributions to his specialty. A host of friends, patients, and associates will miss him sorely. He will be remembered as a doctor and a friend who gave a great deal to a great many.

FRED O. COE, M.D.

ANNOUNCEMENTS AND BOOK REVIEWS

AMERICAN RADIUM SOCIETY

At the Forty-third Annual Meeting of the American Radium Society, May 11-13, 1961, at Colorado Springs, Colo., Robert L. Brown, M.D., Atlanta, Ga., assumed the office of President, succeeding Jesshill Love, M.D., Santa Barbara, Calif. Other officers for the new year include Gilbert H. Fletcher, M.D., Houston, Texas, President-Elect; Ralph F. Phillips, M.D., New York, N. Y., 1st Vice-President; Ethlyn Trapp, M.D., Vancouver, B. C., 2d Vice-President; Joseph H. Farrow, M.D., New York, N. Y., Treasurer; Charles Stetson, M.D., Englewood Hospital, Englewood, N. J., Secretary.

Highlights of the meeting were the election to Honorary Membership of Dr. A. Ennuyer, Chief of Service of Radiotherapy, Radium Institute, University of Paris, France, and the delivery of the Janeway Lecture by Clifford Ash, M.D., Director of the Ontario Cancer Institute, Toronto, Ont., Canada. His subject was "Oral Cancer: A Twenty-Five Year Study."

The Forty-fourth Annual Meeting will be held April 2-4, 1962, at the Waldorf-Astoria Hotel, New York, N. Y.

ARIZONA RADIOLOGICAL SOCIETY

Newly elected officers of the Arizona Radiological Society are: President, Herbert D. Welsh, M.D., Tucson; Vice-President, Marcy L. Sussman, M.D., Phoenix; Secretary-Treasurer, Don E. Matthiesen, M.D., 926 East McDowell Road, Phoenix.

COLORADO RADIOLOGICAL SOCIETY

The following officers will serve the Colorado Radiological Society for the coming year: Emanuel Salzman, M.D., of Denver, President; Stuart Patterson, M.D., of Fort Collins, President-Elect; Seward Imes, M.D., 1845 High St., Denver, Secretary; Cyrus Partington, M.D., of Colorado Springs, Treasurer.

The Society meets on the third Friday of each month, September through May, at the Denver Athletic Club.

IDAHO STATE RADIOLOGICAL SOCIETY

At a recent meeting of the Idaho State Radiological Society in Boise, the following officers were elected: President-Elect, Robert Butz, M.D., Idaho Falls; Secretary-Treasurer, George H. Harris, M.D., Bannock Memorial Hospital, Pocatello; Executive Committee Member, Wesley Levi, M.D., Boise. The President of the Society is Paul Heuston, M.D., Twin Falls.

Society meetings are held twice annually, in the Spring and in the Fall.

ILLINOIS RADIOLOGICAL SOCIETY

Recently elected officers of the Illinois Radiological Society, who will serve until 1963, are: Stephen L. Casper, M.D., Quincy, President; Alden J. Rarick, M.D., Danville, President-Elect; George A. Miller, M.D., Carle Hospital Clinic, Urbana, Secretary-Treasurer.

PHILADELPHIA ROENTGEN RAY SOCIETY

At a May 1961 meeting, the Philadelphia Roentgen Ray Society elected to office Francis Mahoney, M.D., President; George Stein, M.D., Vice-President; Robert B. Funch, M.D., Germantown Dispensary and Hospital, Philadelphia 44, Secretary; Luther Brady, M.D., Treasurer; Councilor-at-Large, Roderick Tondreau, M.D.

TRI-STATE RADIOLOGICAL SOCIETY

The Tri-State Radiological Society at a recent meeting elected the following officers, all from Evansville, Ind.: President, James R. Mathews, M.D.; Vice-President, H. H. Dunham, M.D.; Secretary-Treasurer, John Marchand, M.D., 420 Cherry St. Evansville.

Meetings are held at the Elks' Club in Evansville, the third Wednesday (formerly the fourth Wednesday) of January, March, May, and October.

ELECTRONIC COMPUTER IN COMPILATION OF CANCER DATA

At a national conference of the Society of University Radiologists in May, a report was made by Dr. Philip Rubin, Chief of the Division of Radiation Therapy and Radioisotopes and Director of the Radiation Therapy Center at the University of Rochester School of Medicine and Dentistry, of utilization of the IBM 650 computer to record detailed information on the symptoms and course of cancer of the lungs, bladder, cervix, and ovaries in hundreds of patients. This has made possible the acquisition of an enormous volume of significant data that would otherwise be too unwieldy to handle. Associated with Dr. Rubin in this work were Dr. Lee B. Lusted and Elton Homan.

It is proposed that other university medical centers adopt this system for recording cancer data, which could then be sent to the University of Rochester for processing. Such information would be valuable in analyzing various aspects of cancer diagnosis and treatment.

LECTURES BY DR. BENJAMIN FELSON MEXICO CITY

The Medical Society and the X-Ray Department of the Mexico City General Hospital have invited

Benjamin Felson, M.D., to give a series of evening lectures, Oct. 23-26, 1961, on Thoracic Roentgen Diagnosis: Lungs and Heart. The lectures will be given in English. The fee is 200.00 pesos (\$16.00).

Further information may be obtained from Sociedad Médica del Hospital General, Dr. Balmis 148, México 7, D. F.

TO BE NOTED

Through an unfortunate error, the name of John H. Felts, M.D., Assistant Professor of Internal Medicine, Bowman Gray School of Medicine, was not included as a co-author of the article on "Experimental Comparison of Ortho-Iodohippuric Acid and Iodopyracet in Renal Function Evaluation" in RADIOLOGY for March 1961 (page 464). We regret this omission.

Books Received

Books received are acknowledged under this heading, and such notice may be regarded as recognition of the courtesy of the sender. Reviews will be published in the interest of our readers and as space permits.

RADIOACTIVITY IN MAN: WHOLE BODY COUNTING AND EFFECTS OF INTERNAL GAMMA RAY-EMITTING RADIOISOTOPES. A SYMPOSIUM HELD AT THE VANDERBILT UNIVERSITY SCHOOL OF MEDICINE. Edited by GEORGE R. MENEELY, M.D. A volume of 492 pages, with figures and tables. Published by Charles C Thomas, Springfield, Ill., 1961. Price \$16.50.

INTRODUCTORY MANUAL ON THE CONTROL OF HEALTH HAZARDS FROM RADIOACTIVE MATERIALS. By the COMMITTEE ON PROTECTION AGAINST IONIZING RADIATIONS. Medical Research Council Memorandum No. 39. A pamphlet of 22 pages, with 7 tables. Published by Her Majesty's Stationery Office, London, England, 1961. Price 1s. 9d.

IXTH INTERNATIONAL CONGRESS OF RADIOLOGY 23. VII.—30. VII. 1959 IN MÜNCHEN. ABHANDLUNGEN—TRANSACTIONS—TRAITÉS—ACTAS. Edited by Prof. Dr. B. RAJEWSKY, Dr. phil. nat., Dr. med. h.c., Dr. med. h.c., Frankfurt a. M., Präsident des Kongresses. Editorial Committee: Prof. Dr. J. Becker, Heidelberg, Prof. Dr. R. Glauner, Stuttgart, Prof. Dr. H. Langendorf, Freiburg/B., Prof. Dr. H. Meyer, Marburg/L., Prof. Dr. H. Muth, Homburg/Saar. Secretary to the Editorial Committee: Prof. Dr. F. J. Strnad, Frankfurt a. M. Two volumes of 1,626 pages in all, with 1,008 figures. Published by Georg Thieme, Stuttgart, Germany, in co-operation with Urban & Schwarzenberg, Munich and Berlin,

Germany, 1961. Distributed in the United States and Canada by the Intercontinental Medical Book Corporation, New York 16, N. Y. Price DM 240.—(\$60.00)

DIE ERKRANKUNGEN DER GALLENWEGE UND DES PANKREAS: DIAGNOSTIK, KLINIK UND CHIRURGISCHE THERAPIE. By Priv.-Doz. Dr. med. WALTER HESS, Dozent für Chirurgie an der Universität Basel, em. Professor für Chirurgie an der Universität Alexandria. Drawings by I. Schaumburg, Hamburg. A volume of 672 pages, with 518 illustrations on 267 figures and 42 tables. Published by Georg Thieme, Stuttgart, Germany, 1961. Distributed in the United States and Canada by the Intercontinental Medical Book Corporation, New York 16, N. Y. Price DM 142.—(\$35.50)

HARTSTRAHLTECHNIK. By Dr. med. WOLFGANG FRIK, Privatdozent der med. Strahlenkunde, Med. Klinik mit Poliklinik der Universität Erlangen (Direktor Prof. Dr. N. Henning). A monograph of 144 pages, with 100 illustrations on 76 figures. Published by Georg Thieme, Stuttgart, Germany, 1961. Distributed in the United States and Canada by the Intercontinental Medical Book Corporation, New York 16, N. Y. Price DM 28.50 (\$7.15)

DIE PRÄOPERATIVE RÖNTGENBESTRAHLUNG DES MAMMAKARZINOMS. By Dr. E. MUNTEAN, Universitätsdozent, Graz. A monograph of 108 pages, with 9 figures and 26 tables. Published by Georg Thieme, Stuttgart, Germany, 1961. Distributed in the United States and Canada by the Intercontinental Medical Book Corporation, New York 16, N. Y. Price DM 17.50—(\$4.40)

LE COUDE EN PRATIQUE RHUMATOLOGIQUE. By S. DE SÈZE and M. MAITRE. A monograph of 148 pages, with 105 figures. Published by Masson et Cie, 120, Boulevard Saint-Germain, Paris VI^e, France, 1960. Price 34 NF.

ÉLÉMENTS DE RADIOBIOLOGIE APPLIQUÉE. By ROLAND BUCHET, Médecin radiologiste des hôpitaux de Paris, with the collaboration of G. BREITMAN, Attaché d'électroradiologie des hôpitaux de Paris. Preface by P^r A. Lacassagne. A monograph of 190 pages, with 127 figures. Published by Masson et Cie, 120, Boulevard Saint-Germain, Paris VI^e, France, 1960. Price 29 NF.

Book Reviews

ATLAS DER ANGIOKARDIOGRAPHIE ANGEBORENER HERZFEHLER. By Dr. RALPH KÜNZLER and Dr. NIKOLAUS SCHAD, Assistenten der medizinischen und chirurgischen Abteilung der Universi-

täts-Kinderklinik Zürich. With a foreword by Prof. Dr. Guido Fanconi, Direktor der Universitäts-Kinderklinik Zürich and Prof. Dr. Max Grob, Chefarzt der Chir. Abteilung der Universitäts-Kinderklinik Zürich. Fortschr. a. d. Geb. d. Röntgenstrahlen, Ergänzungsband 86. A volume of 224 pages, with 416 illustrations on 91 figures. Published by Georg Thieme, Stuttgart, Germany, 1960. Distributed in the United States and Canada by the Intercontinental Medical Book Corporation, New York 16, N. Y. Price DM 85.—(\$20.25); to subscribers to the Fortschritte, DM 76.50 (\$18.20)

This well written atlas represents the first German language publication on the subject of angiocardiology of congenital heart disease. The work is divided into two sections. The first of these, dealing with general aspects, includes an introduction,

historical and technical information, results of cardiac catheterization with indications and technique of procedure, normal and abnormal positions of the catheter, normal and diagnostic criteria of pathological angiocardigrams.

In the special section of the text, all types of congenital defects are discussed in great detail, with numerous reproductions, explanatory drawings, and complementary data. This part, comprising 167 pages, is subdivided into five main chapters under the following headings: Stenosis of Pulmonary and Aortic Vessels, Abnormal Intra- and Extracardiac Communications, Transposition of Great Vessels, Pulmonary Circulation—Normal and Abnormal, and Miscellaneous Types. An extensive bibliography is appended.

This concise monograph, combining a well written text with excellent reproductions, should interest pediatricians, cardiologists, and radiologists.



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RADIOLOGICAL SOCIETIES: SECRETARIES AND MEETING DATES

Editor's Note: Secretaries of state and local radiological societies are requested to co-operate in keeping this section up-to-date by notifying the editor promptly of changes in officers and meeting dates.

RADIOLOGICAL SOCIETY OF NORTH AMERICA. *Secretary,* Maurice D. Frazer, M.D., 1744 S. 58th St., Lincoln, Nebr.

AMERICAN RADIUM SOCIETY. *Secretary,* Charles C. Stetson, M.D., Englewood Hospital, Englewood, N. J. Next Annual Meeting, Waldorf-Astoria Hotel, New York, April 2-4 1962.

AMERICAN ROENTGEN RAY SOCIETY. *Secretary,* C. Allen Good, M.D., Mayo Clinic, Rochester, Minn. Next Annual Meeting, Miami Beach, Sept. 26-29, 1961.

AMERICAN COLLEGE OF RADIOLOGY. *Exec. Secretary,* William C. Stronach, 20 N. Wacker Dr., Chicago 6.

AMERICAN CLUB OF THERAPEUTIC RADIOLOGISTS. *Secretary,* Juan A. del Regato, M.D., 2200 North Cascade Ave., Colorado Springs, Colo.

ASSOCIATION OF UNIVERSITY RADIOLOGISTS. *Secretary-Treasurer,* Melvin M. Figley, M.D., 7010 51st Ave., N.E., Seattle, Wash.

SECTION ON RADIOLOGY, A. M. A. *Secretary,* T. Leucutia, M.D., 10 Peterboro, Detroit 1, Mich.

SOCIETY OF NUCLEAR MEDICINE. *Secretary,* Robert W. Lackey, M.D., 452 Metropolitan Bldg., Denver 2, Colo.

SOCIETY FOR PEDIATRIC RADIOLOGY. *Secretary-Treasurer,* Richard D. Lester, M.D., 412 Union St., S. E., Minneapolis 14, Minn.

Alabama

ALABAMA RADIOLOGICAL SOCIETY. *Secretary-Treasurer,* J. Garland Wood, Jr., M.D., Medical College of Alabama, Birmingham 3.

Arizona

ARIZONA RADIOLOGICAL SOCIETY. *Secretary-Treasurer,* Don E. Matthiesen, M.D., 926 E. McDowell Rd., Phoenix. Annual meeting with State Medical Association; interim meeting in December.

Arkansas

ARKANSAS RADIOLOGICAL SOCIETY. *Secretary-Treasurer,* J. B. Scruggs, M.D., 1700 W. 13th St., Little Rock. Meets quarterly.

California

CALIFORNIA MEDICAL ASSOCIATION, SECTION ON RADIOLOGY. *Secretary,* William H. Graham, M.D., 630 E. Santa Clara St., San Jose.

EAST BAY ROENTGEN SOCIETY. *Secretary,* Dan Tucker, M.D., 434 30th St., Oakland 9. Meets monthly, first Thursday, at Peralta Hospital.

LOS ANGELES RADIOLOGICAL SOCIETY. *Secretary,* Walter L. Stilson, M.D., 1720 Brooklyn Ave., Los Angeles 33. Meets second Wednesday, September, November, January, April, and June, Los Angeles County Medical Association Building.

NORTHERN CALIFORNIA RADIOLOGICAL SOCIETY. *Secretary,* Rob H. Kirkpatrick, M.D., 1219 28th St., Sacramento 16. Meets last Monday of each month, September through June.

PACIFIC ROENTGEN SOCIETY. *Secretary,* L. Henry Garland, M.D., 450 Sutter St., San Francisco 8. Meets annually with State Medical Association.

RADIOLOGICAL SOCIETY OF SOUTHERN CALIFORNIA. *Secretary,* Joseph F. Linsman, M.D., 436 N. Roxbury Dr., Beverly Hills.

REDWOOD EMPIRE RADIOLOGICAL SOCIETY. *Secretary,* Lee E. Titus, M.D., 164 W. Napa Street, Sonoma, Calif. Meets second Monday every other month.

SAN DIEGO RADIOLOGICAL SOCIETY. *Secretary,* Stanley A. Moore, M.D., 2466 First Ave., San Diego 1. Meets first Wednesday of each month.

SAN FRANCISCO RADIOLOGICAL SOCIETY. *Secretary-Treasurer,* Merrell A. Sisson, M.D., 450 Sutter St., San Francisco 8. Meets quarterly.

SOUTH BAY RADIOLOGICAL SOCIETY. *Secretary,* Stanford B. Rossiter, M.D., 1111 University Dr., Menlo Park. Meets second Wednesday every month.

Colorado

COLORADO RADIOLOGICAL SOCIETY. *Secretary,* Seward Imes, M.D., 1845 High St., Denver. Meets monthly, third Friday, September through May, at Denver Athletic Club.

Connecticut

CONNECTICUT STATE MEDICAL SOCIETY, SECTION ON RADIOLOGY. *Secretary-Treasurer,* Wayne P. Whitcomb, M.D., Hospital of St. Raphael, New Haven. Meets bimonthly, second Wednesday.

District of Columbia

RADIOLOGICAL SECTION, DISTRICT OF COLUMBIA MEDICAL SOCIETY. *Secretary-Treasurer,* William E. Sheely, M.D., 1746 K St., N.W., Washington 6. Meets third Wednesday, January, March, May, and October, in the Medical Society Library.

Eastern States

EASTERN RADIOLOGICAL SOCIETY. *Secretary-Treasurer,* John D. Osmond, Jr., M.D., 101 E. 185th St., Cleveland, Ohio.

Florida

FLORIDA RADIOLOGICAL SOCIETY. *Secretary,* Richard D. Shapiro, M.D., 1680 Meridian Ave., Miami Beach.

FLORIDA WEST COAST RADIOLOGICAL SOCIETY. *Secretary-Treasurer,* Joseph C. Rush, M.D., 1800 Druid Road, Clearwater. Meets quarterly at the Tampa Terrace Hotel.

GREATER MIAMI RADIOLOGICAL SOCIETY. *Secretary-Treasurer*, Carl E. Balli, M.D., 907-8 Huntington Medical Bldg., Miami 32. Meets monthly, third Wednesday, 8:00 P.M., at Jackson Memorial Hospital.

NORTH FLORIDA RADIOLOGICAL SOCIETY. *Secretary*, Charles H. Newell, M.D., 800 Miami Road, Jacksonville 7. Meets quarterly, March, June, September, and December.

Georgia

ATLANTA RADIOLOGICAL SOCIETY. *Secretary-Treasurer*, Wilson T. Edenfield, M.D., 1026 Scott Circle, Decatur. Meets second Friday, September to May.

GEORGIA RADIOLOGICAL SOCIETY. *Secretary-Treasurer*, George W. Brown, M.D., 317 S. 8th St., Griffin, Ga. Meets in November and at the annual meeting of the State Medical Association.

RICHMOND COUNTY RADIOLOGICAL SOCIETY. *Secretary*, Wm. F. Hamilton, Jr., M.D., University Hospital, Augusta. Meets first Thursday of each month.

Hawaii

RADIOLOGICAL SOCIETY OF HAWAII. *Secretary-Treasurer*, Philip S. Arthur, M.D., 274 Young Hotel Bldg., Honolulu. Meets third Monday of each month.

Idaho

IDAHO STATE RADIOLOGICAL SOCIETY. *Secretary-Treasurer*, George H. Harris, M.D., Bannock Memorial Hospital, Pocatello. Meets in Spring and Fall.

Illinois

CHICAGO ROENTGEN SOCIETY. *Secretary-Treasurer*, William F. Hutson, M.D., 5145 N. California Ave., Chicago 25. Meets at the Sheraton Hotel, second Thursday of October, November, January, February, March, and April at 8:00 P.M.

ILLINOIS RADIOLOGICAL SOCIETY. *Secretary-Treasurer*, George A. Miller, M.D., Carle Hospital Clinic, Urbana. Spring and Fall meetings.

ILLINOIS STATE MEDICAL SOCIETY, SECTION ON RADIOLOGY. *Secretary*, William Meszaros, M.D., 1825 W. Harrison St., Chicago.

Indiana

INDIANA ROENTGEN SOCIETY. *Secretary-Treasurer*, David E. Wheeler, M.D., 1500 North Ritter Ave., Indianapolis. Meets twice a year, first Sunday in May and during fall meeting of State Medical Association.

TRI-STATE RADIOLOGICAL SOCIETY (Southern Indiana, Northwestern Kentucky, Southeastern Illinois). *Secretary-Treasurer*, John Marchand, M.D., 420 Cherry St., Evansville, Ind. Meets third Wednesday, October, January, March, and May.

Iowa

IOWA RADIOLOGICAL SOCIETY. *Secretary-Treasurer*, L. L. Maher, M.D., 1419 Woodland Ave., Des Moines 14. Meets during annual session of State Medical Society, and in the Fall.

Kansas

KANSAS RADIOLOGICAL SOCIETY. *Secretary-Treasurer*, Roger K. Wallace, M.D., Riley County Hospital, Manhattan. Meets in the Spring with the State Medical Society and in the Winter on call.

Kentucky

KENTUCKY RADIOLOGICAL SOCIETY. *Secretary-Treasurer*, Robert H. Akers, M.D., VA Hospital, Louisville 2. Meets monthly, second Friday, at Seelbach Hotel, Louisville.

Louisiana

ORLEANS PARISH RADIOLOGICAL SOCIETY. *Secretary*, Joseph V. Schlosser, M.D., Charity Hospital of Louisiana, New Orleans 13. Meets second Tuesday of each month.

RADIOLOGICAL SOCIETY OF LOUISIANA. *Secretary-Treasurer*, Robyn Hardy, M.D., 4324 Magnolia St., New Orleans 15.

SHREVEPORT RADIOLOGICAL CLUB. *Secretary*, W. R. Harwell, M.D., 608 Travis St. Meets monthly September to May, third Wednesday.

Maine

MAINE RADIOLOGICAL SOCIETY. *Secretary-Treasurer*, Albert A. Poulin, M.D., Thayer Hospital, Waterville. Meets in June, October, December, and April.

Maryland

MARYLAND RADIOLOGICAL SOCIETY. *Secretary*, Albert B. Shackman, M.D., 705 Medical Arts Bldg., Baltimore 1.

Michigan

DETROIT X-RAY AND RADIUM SOCIETY. *Secretary-Treasurer*, Kenneth L. Krabbenhoft, M.D., 3825 Brush, Detroit 1. Meets first Thursday, October to May, Wayne County Medical Society rooms.

UPPER PENINSULA RADIOLOGICAL SOCIETY. *Secretary*, Arthur Gonty, M.D., Menominee. Meets quarterly.

Minnesota

MINNESOTA RADIOLOGICAL SOCIETY. *Secretary-Treasurer*, Donald H. Peterson, M.D., 25 W. Fourth St., St. Paul 2. Meets Fall, Winter, and Spring.

Mississippi

MISSISSIPPI RADIOLOGICAL SOCIETY. *Secretary-Treasurer*, Jack K. Goodrich, M.D., University of Mississippi Medical Center, Jackson. Meets monthly, on third Thursday, 6:00 P.M., at Hotel Edwards, Jackson.

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Missouri

GREATER ST. LOUIS SOCIETY OF RADIOLOGISTS. *Secretary-Treasurer*, William E. Powers, M.D., 510 S. Kingshighway, St. Louis 10. Meets on fourth Wednesday, October to May.

MISSOURI RADIOLOGICAL SOCIETY. *Secretary-Treasurer*, Milton Shoss, M.D., 937 Broadway, Cape Girardeau.

RADIOLOGICAL SOCIETY OF GREATER KANSAS CITY. *Secretary*, J. Stewart Whitmore, M.D., 1010 Rialto Bldg., Kansas City 6, Mo. Meets fourth Friday of each month October through May.

Montana

MONTANA RADIOLOGICAL SOCIETY. *Secretary-Treasurer*, J. K. Boughn, M.D., 35—11th Ave., Helena. Meets annually.

Nebraska

NEBRASKA RADIOLOGICAL SOCIETY. *Secretary-Treasurer*, Ronald E. Waggener, M.D., Nebraska Methodist Hospital, Omaha. Meets third Wednesday of each month at 6 P.M. in Omaha or Lincoln.

Nevada

NEVADA RADIOLOGICAL SOCIETY. *Corresponding Secretary*, Robert M. Taylor, M.D., 2020 W. Charleston Blvd., Las Vegas. Meets during annual session of State Medical Society.

New England

CONNECTICUT VALLEY RADIOLOGIC SOCIETY. *Secretary-Treasurer*, James L. Krieger, M.D., 85 Jefferson St., Hartford 6, Conn. Meets second Friday of October and April.

NEW ENGLAND ROENTGEN RAY SOCIETY. *Secretary*, Robert E. Wise, M.D., 605 Commonwealth Ave., Boston 15, Mass. Meets third Friday, October through May, Longwood Towers, Brookline, Mass.

New Hampshire

NEW HAMPSHIRE ROENTGEN RAY SOCIETY. *Secretary-Treasurer*, Paul Y. Hasserjian, M.D., 1470 Elm St., Manchester. Meets three times a year.

New Jersey

RADIOLOGICAL SOCIETY OF NEW JERSEY. *Secretary*, George H. Burke, M.D., 601 Grand Ave., Asbury Park. Annual meeting in Spring, Atlantic City; Fall meeting October or November, Newark.

New Mexico

NEW MEXICO ASSOCIATION OF RADIOLOGISTS AND PATHOLOGISTS. *Secretary-Treasurer*, George C. Chaney, M.D., 801 Encino Pl., N.E., Albuquerque.

New York

BROOKLYN RADIOLOGICAL SOCIETY. *Secretary-Treasurer*, Joseph P. Arcomano, M.D., 168 Clinton St., Brooklyn 1. Meets first Thursday of each month, October through May.

BUFFALO RADIOLOGICAL SOCIETY. *Secretary*, Kenneth H. Seagrave, M.D., Buffalo Medical Group, 537 Delaware Ave., Buffalo 2. Meets second Monday, October to May.

CENTRAL NEW YORK RADIOLOGICAL SOCIETY. *Secretary*, Joseph A. Head, M.D., Hospital of the Good Shepherd, Syracuse University, Syracuse. Meets first Monday, October through May.

KINGS COUNTY RADIOLOGICAL SOCIETY. *Secretary-Treasurer*, C. P. Naidorf, M.D., 411 Parkside Ave., Brooklyn 26. Meets fourth Thursday, October to April (except December), at 9:00 P.M., Kings County Medical Bldg.

NASSAU RADIOLOGICAL SOCIETY. *Secretary*, Robert Tugendhaft, M.D., Meadowbrook Hospital, Hempstead. Meets second Tuesday, February, April, June, October, and December.

NEW YORK ROENTGEN SOCIETY. *Secretary*, Bernard S. Wolf, M.D., 11 E. 100th St., New York 29.

NORTHEASTERN NEW YORK RADIOLOGICAL SOCIETY. *Secretary-Treasurer*, Lester I. Citren, M.D., St. Mary's Hospital, Troy. Meets in the capital area second Wednesday, October, November, March, and April; annual meeting, May or June.

RADIOLOGICAL SOCIETY OF STATE OF NEW YORK. *Secretary-Treasurer*, John W. Colgan, M.D., 273 Hollywood Ave., Rochester 18. Meets annually with the State Medical Society.

ROCHESTER ROENTGEN-RAY SOCIETY. *Secretary-Treasurer*, Robert H. Greenlaw, M.D., 260 Crittenden Blvd., Rochester 20. Meets last Monday of each month, September through May.

WESTCHESTER RADIOLOGICAL SOCIETY. *Secretary*, Anthony A. Maglione, M.D., 27 Ludlow St., Yonkers. Meets third Tuesday of January and October and as announced.

North Carolina

RADIOLOGICAL SOCIETY OF NORTH CAROLINA. *Secretary-Treasurer*, A. Bascom Croom, M.D., 1102 Greenway Dr., High Point. Meets Spring and Fall of each year.

North Dakota

NORTH DAKOTA RADIOLOGICAL SOCIETY. *Secretary*, Richard F. Raasch, M.D., P.O. Box 990, Dickinson. Meets in the Spring with State Medical Association; in Fall or Winter on call.

Ohio

OHIO STATE RADIOLOGICAL SOCIETY. *Secretary*, Paul D. Meyer, M.D., 6160 Cherry Hill Dr., Columbus.

CENTRAL OHIO RADIOLOGICAL SOCIETY. *Secretary-Treasurer*, Robert L. Friedman, M.D., Grant Hospital, Columbus 15. Meets second Thursday, October, November, January, March, and May, Columbus.

CLEVELAND RADIOLOGICAL SOCIETY. *Secretary-Treasurer*, Norman E. Berman, M.D., 14404 S. Park

Blvd., Shaker Heights 20. Meets at 7:00 P.M., fourth Monday, October, November, January, February, March, April.

GREATER CINCINNATI RADIOLOGICAL SOCIETY. *Secretary-Treasurer*, W. Donald Janny, M.D., 722 Scott St., Covington, Ky. Meets first Monday, September through May, at Cincinnati General Hospital.

MIAMI VALLEY RADIOLOGICAL SOCIETY. *Secretary-Treasurer*, William D. Roberts, M.D., 1030 Reibold Bldg., Dayton 2, Ohio. Meets second Thursday of each month, at Miami Valley Hospital, Dayton.

Oklahoma

OKLAHOMA STATE RADIOLOGICAL SOCIETY. *Secretary*, Simon Pollack, M.D., Utica Square Medical Center, Tulsa. Meets in January, May, and October.

Oregon

OREGON RADIOLOGICAL SOCIETY. *Secretary-Treasurer*, George R. Satterwhite, M.D., 1123 S.W. Yamhill St., Portland. Meets monthly, second Wednesday, October to June, at the University Club, Portland.

Pacific Northwest

PACIFIC NORTHWEST RADIOLOGICAL SOCIETY. *Secretary-Treasurer*, John W. Burkey, M.D., 509 Olive Way, Seattle 1, Wash.

Pennsylvania

PENNSYLVANIA RADIOLOGICAL SOCIETY. *Secretary-Treasurer*, Frederick R. Gilmore, M.D., Clearfield Hospital, Clearfield. Next annual meeting, Pocono Manor Inn, May 25-26, 1962.

PHILADELPHIA ROENTGEN RAY SOCIETY. *Secretary*, Robert B. Funch, M.D., Germantown Hospital, Philadelphia 44. Meets first Thursday of each month at 5:00 P.M., from October to May, in Thompson Hall, College of Physicians.

PITTSBURGH ROENTGEN SOCIETY. *Secretary*, Ross H. Smith, Jr., M.D., St. Margaret Memorial Hospital, Pittsburgh 1. Meets monthly, second Wednesday, October through June.

Rocky Mountain States

ROCKY MOUNTAIN RADIOLOGICAL SOCIETY. *Secretary-Treasurer*, John H. Freed, M.D., 4200 E. Ninth Ave., Denver 20, Colo. Next annual meeting, Denver Hilton Hotel, Denver, Colo., Aug. 10-12, 1961.

South Carolina

SOUTH CAROLINA RADIOLOGICAL SOCIETY. *Secretary-Treasurer*, George W. Brunson, M.D., 1406 Gregg St., Columbia. Meets (primarily for business) in conjunction with South Carolina Medical Association in May. Scientific meeting in Fall.

South Dakota

RADIOLOGICAL SOCIETY OF SOUTH DAKOTA. *Secretary-Treasurer*, Donald J. Peik, M.D., 303 S. Minnesota Ave., Sioux Falls. Meets during annual meeting of State Medical Society.

The Southeast

SOUTHERN RADIOLOGICAL CONFERENCE. *Secretary-Treasurer*, Marshall Eskridge, M.D., 1252 Springhill Ave., Mobile, Ala.

The Southwest

SOUTHWESTERN RADIOLOGICAL SOCIETY. *Secretary-Treasurer*, Ralph S. Clayton, M.D., 1501 Arizona Bldg. 2 A, El Paso, Texas. Meets monthly, last Friday, 6:30 P.M., Paso Del Norte Hotel, El Paso.

Tennessee

EAST TENNESSEE RADIOLOGICAL SOCIETY. *Secretary-Treasurer*, J. Marsh Frere, Jr., M.D., 205 Medical Arts Bldg., Knoxville. Meets in September and January, and prior to State Medical Association meeting.

MEMPHIS ROENTGEN SOCIETY. *Secretary-Treasurer*, Hollis H. Halford, M.D., Kennedy VA Hospital, Memphis 15. Meets monthly first Monday, John Gaston Hospital.

TENNESSEE RADIOLOGICAL SOCIETY. *Secretary-Treasurer*, B. M. Brady, Jr., M.D., St. Joseph Hospital, Memphis, Tenn. Meets annually with State Medical Association in April.

Texas

CENTRAL TEXAS RADIOLOGICAL SOCIETY. *Secretary-Treasurer*, Glenn Addison Stokdyk, M.D., VA Center, Temple. Meets monthly, fourth Monday, at Kosel's Cafe, Temple.

DALLAS-FORT WORTH RADIOLOGICAL SOCIETY. *Secretary-Treasurer*, Frederick J. Bonte, M.D., 5201 Harry Hines Blvd., Dallas 35. Meets monthly, third Monday, 6:30 P.M., at the Greater Fort Worth International Airport.

HOUSTON RADIOLOGICAL SOCIETY. *Secretary*, John Douglas Reeve, M.D., Jesse H. Jones Library Bldg., Houston 25. Meets monthly, last Monday, at Doctors' Club.

SAN ANTONIO-MILITARY RADIOLOGICAL SOCIETY. *Secretary*, Hugo F. Elmendorf, Jr., M.D., 730 Medical Arts Bldg., San Antonio 5, Texas. Meets at Fort Sam Houston Officers' Club, third Wednesday of each month, 6:30 P.M.

TEXAS RADIOLOGICAL SOCIETY. *Secretary-Treasurer*, R. P. O'Bannon, M.D., 1216 Pennsylvania Ave., Fort Worth 4. Next meeting in Austin, Jan. 19-20, 1962.

Utah

UTAH STATE RADIOLOGICAL SOCIETY. *Secretary-Treasurer*, Richard Y. Card, M.D., St. Mark's Hospital, Salt Lake City 3. Meets third Wednesday, January, March, May, September, November.

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Vermont

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ROENTGEN DIAGNOSIS

THE HEAD AND NECK

Two Vascular Grooves of the External Table of the Skull Which Simulate Fractures. Herbert Schunk and Yosh Maruyama. *Acta radiol.* 54: 186-194, September 1960. (Massachusetts General Hospital, Boston 14, Mass.)

Two grooves of the external table of the skull commonly mistaken for fractures were studied in a material consisting of roentgenograms of 556 dried skulls, 2,806 clinical skull roentgenograms, and anatomical dissections of cadaver specimens. One of the grooves is observed on the lateral projection in the temporoparietal region and represents a vascular impression caused by the middle temporal artery; the other is seen in the frontal region and is the vascular impression produced by the supraorbital artery.

On the external table of the skull, in the temporoparietal region, a linear groove was observed in 72 per cent of the dried skull specimens; in over half of the number this grooving was bilateral. It originated above the external auditory meatus, near the zygomatic-temporal junction, and extended vertically or semivertically over the squamosal portion of the temporal bone. In only 2 per cent of the dried skulls was the groove deep enough to appear as a line on the roentgenogram. Twenty-seven (1 per cent) of the 2,806 clinical skull roentgenograms showed distinct lines of sufficient clarity to be misinterpreted as fractures; however, faint grooves were seen more frequently. The lower course of the groove may be straight or may exhibit a slight convex posterior or anterior curve. This lowermost portion of the curve can often be demonstrated by a slightly oblique lateral projection; branching was rarely noted. The course in the squamous portion of the temporal bone is linear and straight and intersects the grooves of the middle meningeal vessels on the inner table of the skull. The groove lacks the distinctness of a true recent fracture and, on close inspection, it can be seen that it does not pass completely through the external table. The line is not visible in the anteroposterior plane. If bilateral, the groove should follow a similar course on both sides. The groove was found to be an impression caused by the middle temporal artery.

The second of the grooves investigated occurs in the frontal region; it also can follow a quite linear course. It was encountered less commonly, being found in only 27 per cent of the dried skull specimens. In nearly half of these, it was bilateral. In the great majority of instances, the groove was shallow and broad; multiple, parallel, or branched grooves were frequently observed. The groove originated near the supraorbital foramen in some specimens; in others, as much as 2 to 3 cm. distant from it. The groove extended posteriorly and upward in an oblique fashion toward the coronal suture in the lateral projection. In postero-anterior roentgenograms, the groove begins in the region of the midorbital ridge and ascends almost vertically, but angulates and arches slightly laterally toward the region of the coronal suture. Deep grooves were present in 3 per cent of the dried skulls, but not all were sufficiently linear or unbranched that they could be mistaken for fracture lines. Ten of the 2,806 clinical skull roentgenograms (less than 1 per cent) revealed grooves which simulated fracture lines. Differentiation from true fracture is easier when the grooves occur bilaterally and have a symmetrical

course. As mentioned above, this groove is the vascular impression caused by the supraorbital artery.

Ten roentgenograms; 6 photographs; 4 diagrams; 1 table.

SAMUEL B. HAVESON, M.D.

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Percutaneous Injection of the Thalamus in Parkinsonism. A Preliminary Report: Relief of Bilateral Facial Grimaces. Arthur Ecker and Theodore Perl. *Arch. Neurol.* 3: 271-278, September 1960. (407 University Ave., Syracuse 10, N. Y.)

A new method of injecting the region of the ventrolateral nucleus of the thalamus, under radiologic control, is described. The target point is selected on plain radiographs of the skull if the pineal body is calcified, or on pneumoencephalograms if it is not. With the assistance of the radiographs, the target is projected through the center of the foramen ovale onto the skin, thus determining the entry point and direction of the needle. Under local anesthesia, a 21-gauge, 4-inch guide needle is introduced just through the foramen ovale. Through the guide needle, a 26-gauge needle, 6 inches long, is inserted the calculated distance to the target. After 0.2 c.c. of local anesthetic is injected into the brain, one or more times, with beneficial results and without complications, a mixture of absolute alcohol (5 parts) and radiopaque material (sodium diatrizoate or methylglucamine diatrizoate, 1 part) is introduced in units of 0.1 or 0.2 c.c. When maximal benefit is obtained, or any complication develops, the procedure is concluded by withdrawing the needles.

This method seems to have the following advantages: (1) absence of general anesthesia; (2) avoidance of a bur hole in the skull; (3) use of a very fine needle, to penetrate the brain, minimizing the risk of hemorrhage in the basal ganglia; (4) full exposure of head, permitting accurate radiography.

The procedure has been employed in 7 patients to date. Injections were made in the thalamus of only one side. In all cases, contralateral rigidity and tremor were largely or completely relieved for seven to eighteen months (average fifteen months). In 2 patients the injections were repeated on the same side because of recurrence of symptoms. Two patients also had relief of involuntary bilateral movements of the lips and tongue. The only serious complication was the production of permanent hemiplegia in 1 case, resulting from avoidable technical errors. In this instance, a single injection of 0.8 c.c. of the alcohol-sodium diatrizoate mixture was injected; injection of only 0.1 or 0.2 c.c. at a time is now recommended.

Five roentgenograms; 1 sketch; 1 table.

RICHARD A. ELMER, M.D.

Atlanta, Ga.

Radiographic Investigation of Facial Asymmetry. A Study of Projection Factors Involved in Determining the So-Called "Camper Plane." E. Koivisto, G. Lindblom, L. Pyrkönen, and C. Wegelius. *Brit. J. Radiol.* 33: 508-511, August 1960. (Norrstull's Hospital, Stockholm, Sweden)

In the performance of measurements on human skulls, some arbitrary lines are often referred to; the ones most commonly used in odontology are the Camper line or plane and the Frankfort line or plane.

The Frankfort line passes from the lowest point on

the orbital border (orbitale) to that point on the margin of the external auditory meatus which lies vertically above the center of the meatus (porion). Owing to the asymmetry of the skull, however, the right and left lines are usually not situated in the same plane. Hence, the Frankfort plane is defined by three points, the two poria and the left orbitale. The Camper line is roughly parallel with the zygomatic arch, the occlusal plane, and also with the horizontal level, when body and head are kept erect in a physiological rest position. Unfortunately, it is not as rigidly defined as the Frankfort line. The anterior point is varying given as the lowest point on the base of the nasal spine, the nasal spine, or the base of the nasal wings. The posterior point is given as the lower or upper border of the auditory meatus, the tip or the center of the tragus, or somewhere on its base. Lindblom has suggested that the Camper line be defined as "a line connecting the posterior part of the lower border of the wing of the nose to the center of the tragus."

The authors discuss the projection factors involved in determining the so-called "Camper plane." The analysis includes not only direct radiography but also possible additive misleading effects made clear by the use of photofluorographic recording. The incidence of facial asymmetry in an unselected material consisting of 114 women, aged thirty-three to ninety years, was found to be 26 per cent.

Two roentgenograms; 3 photographs; 1 graph.

Value of Different Projections in Diagnosing Cholesteatoma. Gert Jensen, Chr. Jespersen, and S. Brünner. *Acta radiol.* 54: 177-185, September 1960. (Sundby Hospital, Copenhagen, Denmark)

The relative value of various projections in the diagnosis of [secondary] cholesteatoma is analyzed on the basis of a study of 80 cases of chronic otitis media in which operation revealed bone destruction. Ten of the patients were from six to ten years of age; the majority (62) were over twenty. In 41 cases the cholesteatoma was located in the antrum, in 3 cases in the attic, and in the remaining 36 in both antrum and attic. In 6 cases a fistula running into the lateral semicircular canal was found at operation. Destruction was so widespread in 6 cases that the dura mater overlying the tegmen was exposed.

All of the patients were examined with the Schüller, Runström III, and Chaussé III projections, and bone destruction was diagnosed if there was evidence of it in any one of these projections (70 per cent of the cases). Chaussé's projection contributed most to the diagnosis, i.e., 62 per cent of the cases; bone destruction was noted with Schüller's projection in 40 per cent, and with the Runström III projection in 26.3 per cent. When tomography was performed, the chance of detecting bone destruction with the Chaussé III projection was increased to about 80 per cent.

Eleven roentgenograms; 2 photographs; 3 tables.

THEODORE E. KEATS, M.D.
University of Missouri

Utilization of Roentgenology in the Study of Speech Mechanisms. Carlisle C. Smith, Samuel G. Fletcher, Ralph L. Shelton, Jr., and James F. Bosma. *Am. J. Roentgenol.* 84: 213-219, August 1960. (Salt Lake County General Hospital, Salt Lake City 15, Utah)

New x-ray apparatus and technics permit demonstration of structures and analysis of movements which pre-

viously were inaccessible to study; for example, roentgen procedures are increasingly used in investigating the mechanisms and pathology of speech. The authors describe the equipment, technics, and methods of analysis appropriate to such examination.

Conventional roentgenography is important in the preliminary identification and demonstration of gross structural disturbances. Image amplification and cine-radiography, with synchronous sound recording, are particularly suited to the study of speech. Rapid film or cassette changers provide information and details not shown by the image amplifier. Body-section roentgenography is of special value in visualizing the laryngeal area. The true and false vocal cords can be identified only with difficulty in standard roentgenograms but are well outlined by laminagraphy. The prolonged exposure, however, limits study to static "poses" or sustained phonations.

Film analysis and accurate measurement of the speech structures will usually be the responsibility of the speech pathologist. The radiologist, however, must be prepared to give assistance and advice concerning any phase of the interpretation; particularly may he be of assistance in the identification of anatomic structures, in the evaluation and measurement of image distortion, and in suggesting alterations of position or technic to demonstrate more clearly a movement or structure. Radiation safety and protection are also his responsibility.

A variety of important speech problems are listed which may be evaluated by roentgenography without excessive radiation exposure.

Ten roentgenograms; 5 tracings; 1 photograph; 1 diagram.

JOHN W. WILSON, M.D.
Johnstown, Penna.

Cinefluorography in the Pre- and Post-Operative Management of Laryngeal Cancer. John A. Kirchner, James H. Scatliff, and Donald P. Shedd. *Ann. Otol., Rhin. & Laryng.* 69: 768-780, September 1960. (333 Cedar St., New Haven, Conn.)

Partial laryngectomy or well planned radiotherapy may control or cure cancer in locations where total laryngectomy would involve unnecessary sacrifice of function. The possibility of carrying out function-sparing surgery or irradiation in any particular case depends upon the meticulous study of the size of the tumor, its inferior extent, and the invasion of neighboring tissues. This information frequently cannot be obtained from the endoscopic examination alone, and in the past three years the authors have found cinefluorography increasingly helpful in evaluating the larynx involved by cancer.

The examination consists of motion-picture fluoroscopic recording of the passage of a barium mixture as it passes through the pharynx following oral administration. A Philips' 5-inch image amplifier, a 16-mm. Auricon camera, and linograph ortho film are employed. A recording is made during phonation, inspiration, and the Valsalva maneuver.

Six illustrative cases are reported. In 1 case in which the lesion was difficult to visualize endoscopically, cinefluorography helped corroborate the clinical impression of fixation of the cord and demonstrated a submucosal extension of the tumor. In another case, the lower edge of the tumor was difficult to identify because of bleeding, pain, fragmentation of tissue, etc.; cinefluorography outlined the tumor and showed that the

subglottic area was not involved and that there was no extension into the pre-epiglottic area. This case was therefore considered suitable for radiotherapy.

Cinefluorography has been particularly helpful in the evaluation of complications arising postoperatively, as cough, regurgitation, dysphagia, or recurrent neoplasm. It also affords a means of correlating esophageal voice with various modifications of laryngectomy or laryngopharyngectomy.

Eight roentgenograms; 6 drawings.

DAVID SILVER, M.D.
Los Angeles, Calif.

Soft Tissue Roentgenography: Its Use in Diagnosis of Thyroid Carcinoma. Robert Lloyd Segal, Herman Zuckerman, and Eugene W. Friedman. *J.A.M.A.* **173**: 1890-1894, Aug. 27, 1960. (35 E. 85th St., New York 28, N. Y.)

Thyroid carcinomas sometimes show characteristic calcifications which can be detected by soft-tissue roentgenography. These calcifications, unlike those in benign thyroid lesions, are poorly margined, hazy, not densely calcific, and about equal in size; usually they are grouped in streaks or in a nebular formation within a well limited area which does not have a calcific rim. They are presumably due to the presence of psammoma bodies, which are found on histologic section in about 50 per cent of carcinomas of the thyroid gland.

In 3 of 6 patients who were proved at operation to have carcinoma of the thyroid, preoperative roentgenographic findings would have sufficed to make the diagnosis. In each of the 3 cases psammoma bodies were present in sections of the carcinoma. There were no false-positive results in 23 patients with a variety of benign thyroid conditions.

The technic for soft-tissue roentgenography of the thyroid is described.

Four roentgenograms; 2 tables.

WILLIAM MARTEL, M.D.
University of Michigan

THE CHEST

New Dimensions in Chest Radiography. Lewis E. Etter and Lawrence C. Cross. *Dis. of Chest* **38**: 124-130, August 1960. (University of Pittsburgh School of Medicine, Pittsburgh, Penna.)

The use of 14 × 17-inch films in 15 × 18-inch cassettes for chest radiography has become traditional in the United States, and the necessity for this film size has not been questioned. On a 14 × 17-inch postero-anterior chest film of an average man or woman, however, one sees wasted film above the shoulders and a gray void beneath the diaphragm. Review of the postero-anterior chest roentgenograms of 500 men and 406 women (including 200 pregnant women) revealed that a 14 × 14-inch film would be quite adequate for 98 per cent of the examinations. The economy of reducing the exposed area by approximately 18 per cent is obvious; it is estimated that at current prices this would represent a saving of about \$0.13 per film. Even more important is the reduction of the radiation dose. In the pregnant woman, where the diaphragm is high, and to avoid fetal exposure, an 11 × 14-inch film of the chest would be satisfactory. This film size would also be adequate for the usual anteroposterior lordotic view of the chest. If 3 inches are eliminated at the bottom of the film, usually nothing of value is lost.

Processing hangers for the 14 × 14-inch films are available. A film of this size may be placed in a 15 × 18-inch cassette by pushing it to the hinged end, where the screen pressure will hold it in place. When it becomes necessary to buy new cassettes, only 15 × 15-inch cassettes and screens need be purchased for chest examinations.

When 14 × 17-inch films are used for both abdomen and chest, there is obviously an overlap of radiation in the region of the diaphragm in patients having both of these examinations. Since anything less than a 14 × 17-inch film is not adequate for the adult abdomen, this double exposure can be prevented by employing a 14 × 14-inch chest film with square collimation.

Seven roentgenograms; 3 photographs; 2 graphs.

JOHN F. RIESSER, M.D.
Springfield, Ohio

Value of Angiocardiography in the Study of Pulmonary Abnormalities. Paul Janin. *J. de radiol.* **41**: 432-439, August-September 1960. (In French) (Grenoble, France)

Angiocardiography is important in studying abnormalities of the lung, not only for depicting vascular anomalies but also to show vascular changes which are associated with or might possibly be playing a causative role in other abnormalities of pulmonary tissue.

Cases are grouped in four principal categories: (1) syndromes due to developmental failure, including agenesis, aplasia, or hypoplasia; (2) abnormal localization of bronchopulmonary tissue, particularly sequestration; (3) lung diseases due to bronchial changes, such as air cysts, emphysema, and related conditions; (4) apparently isolated venous abnormalities.

In most cases, the knowledge obtained by angiocardiography is of great value in preoperative evaluation. The procedure frequently gives the surgeon useful information.

Ten roentgenograms; 3 drawings.

CHARLES M. NICE, JR., M.D., Ph.D.
Tulane University

Cavitating Primary Pulmonary Tuberculosis in Infancy. N. Joffe. *Brit. J. Radiol.* **33**: 430-439, July 1960. (Baragwanath Hospital, Johannesburg, Union of South Africa)

The present-day occurrence of primary tuberculous cavitation in infancy is uncommon and there are few references in the literature, particularly the radiological literature, to this form of the progressive primary lesion. Grzybowski (*Tubercle* **35**: 113, 1954) found the great majority of cases of active pulmonary tuberculosis in children fell readily into one of five main groups: (1) simple primary complex; (2) primary tuberculosis with lobar or segmental lesions; (3) pleural effusions; (4) miliary tuberculosis; (5) the adult type of chronic pulmonary tuberculosis, this last-named being practically unknown in the first five years of life.

A study of the primary tuberculous lesions in African children in Kenya (Stephen Carter: *Arch. Dis. Childhood* **29**: 213, 1954) revealed certain differences in the manifestations of the primary lesion in the African child as compared with the European child, the most important being the higher incidence of tuberculous bronchopneumonia. Failure to localize the primary lesion is attributed to the lack of immunity among African children in Kenya, where tuberculosis has been introduced comparatively recently. A somewhat simi-

lar situation exists in South Africa, where primary tuberculosis in the Bantu infant not infrequently progresses to the stage of primary cavitation. Overcrowding and malnutrition probably play a part. The age of the child at the time of the infection is of considerable importance.

The present study is concerned with some of the radiological aspects of cavitating primary tuberculosis detected during the first two years of life, based on a series of 27 cases. Radiologically, the cavity was usually observed as an area of translucency most commonly irregular in outline and lying within a region of homogeneous consolidation. The size of the translucency and the area of consolidation varied considerably, but the latter was usually lobar or sublobar in extent. No clearly defined cavity wall could be detected beyond the irregular, often ragged outline of the translucent area. This type of case was very common and represented breakdown occurring in an acute caseous pneumonia before a protective barrier could be provided for the surrounding lung tissue. In a minority of cases the cavity appeared as a more well defined, spherical, or oval translucency surrounded by a limited area of caseous pneumonia. A not uncommon finding was bulging of an interlobar fissure away from an adjacent area of consolidation. If a tuberculous cavity communicates with a bronchus which is partially occluded so that a check-valve mechanism is set up, the tuberculous cavity may become a tension cavity. Rarely, thin-walled "cysts" may be observed in association with primary tuberculosis in the infant; these thin-walled cavities resemble pneumatoceles.

Other roentgen features associated with cavitation which may be of great importance in arriving at a diagnosis of tuberculosis are: (1) an area of homogeneous consolidation which surrounds the cavity and which is usually lobar or sublobar in extent, or may even involve an entire lung; (2) small areas of consolidation, usually fairly well defined and often rather dense in nature, involving part or all of one or both lung fields; (3) miliary tuberculosis; (4) hilar and/or mediastinal lymphadenopathy; (5) spontaneous pneumothorax (a rather uncommon complication of cavitating tuberculosis in infancy); (6) mediastinal emphysema; (7) pleural effusion, which is distinctly uncommon.

Very few conditions give rise to any difficulty in the differential diagnosis of cavitating primary tuberculosis in infancy. Suppurative pneumonia and lung abscess offer the greatest difficulty to the radiologist. The points to be considered in the differentiation of these conditions are discussed.

Twenty-three roentgenograms; 1 table.

PETER TORBEY, M.D.
University of Washington

Ossifying Pneumonitis and Calcinosis. Report of a Case. Constantine Soter, Y. Berkmen, H. Gür, A. A. Hadzidakis, and John H. Gilmore. *Acta radiol.* 54: 195-203, September 1960. (Illinois Masonic Hospital Association, Chicago, Ill.)

The formation of bone in the lungs is unusual, and the association with massive calcinosis is very rare. The authors report the case of a 50-year-old man who was first seen in December 1954, with a clinical picture of pneumonitis. Tests for psittacosis gave a positive high titer. A chest roentgenogram at that time showed only slight pulmonary fibrosis and cardiac enlargement. Over the next two years the patient became increasingly

dyspneic, and pulmonary function tests revealed a severe reduction in vital capacity and maximum breathing capacity. Serum calcium determinations on several occasions showed a range of 9.2 to 13.9 mg. per cent. Figures for serum phosphorus were 3.8 to 7.0 mg. per cent. On May 9, 1956, a chest roentgenogram was reported as negative. On June 6, a month later, however, examination of the chest showed bilateral parenchymal lesions extending from apices to base and consisting of irregularly disseminated, patchy and nodular masses; by July these had increased in size and extent. A chest roentgenogram obtained a few months prior to the patient's death in 1959, from progressive heart failure, revealed only slight progression of the nodular pulmonary infiltrates. Autopsy disclosed massive calcinosis of the lungs with bone formation in the interstitial connective tissue, including the interalveolar septa. There was also extensive calcification in the arteries and calcification of the gastric mucosa and kidneys. There was no osteoporosis, and the parathyroids were not enlarged; therefore the possibility of hyperparathyroidism is considered unlikely.

The clinical course and the postmortem findings suggest that the original psittacotic pneumonitis produced a severe inflammation of the interstitial tissues of the lung which resulted in unusually marked interstitial fibrosis, further impairing the heart which had already been subject to infarction. Chronic passive congestion ensued and eventually precipitated the ossification and massive calcium deposits. There is considerable evidence that venous stasis or general circulatory impairment favors bone formation provided other conditions favorable to ossification are present (e.g., mitral stenosis). It is considered unlikely that the calcifications occurred first and some of them progressed into formation of bone, since a lung biopsy performed several months before death showed mostly bone formation in the interalveolar septa, and at autopsy the calcifications were overwhelming. The authors believe that the ossifying pneumonitis existed in the lungs even when the chest roentgenograms were considered essentially normal, since these fine bone spicules are not demonstrable roentgenologically, and the chest lesions appeared suddenly when massive precipitation of calcium salts occurred. The two conditions may have been independent, and in the authors' case co-existed by chance, because predisposing factors for both were present.

Four roentgenograms.

SAMUEL B. HAVESON, M.D.
Lynwood, Calif.

Hemorrhagic Varicella Pneumonia. John G. Eswein and Victor P. DiDomenico. *Ann. Int. Med.* 53: 607-613, September 1960. (V.P.D., Worcester City Hospital, Worcester 3, Mass.)

The authors report the case of a 37-year-old white man with hemorrhagic varicella pneumonia treated with cortisone. Chest films showed diffuse, soft, coarsely nodular infiltrates in the lower lung fields, which cleared progressively after treatment.

Although chickenpox is usually benign in adults, it may run a very severe course and may even be fatal. It has been stated that corticosteroids should not be used in varicella pneumonia because of the possibility of reactivating the infection and producing a more severe disease. The mechanism of such complications as viral pneumonitis, hemorrhage, nephrosis, encephalitis, and idiopathic thrombocytopenic purpura, however, is

not at all clear, and they may well represent a hyperimmune reaction either to the varicella virus or products elaborated by it.

Because the authors' patient appeared to be in *ex-tremis*, it was felt that the use of corticosteroids was indicated. The signs and symptoms cleared rapidly within the course of twelve hours after the initiation of this therapy. This is in contrast to the course in other recorded cases, which showed clearing of symptoms by lysis despite all treatment (Southard: *Am. J. Roentgenol.* 76: 533, 1956). It is suggested that the hemorrhagic lesions in the lungs, skin, and gastrointestinal tract may well represent generalized vasculitis, or an immunovascular phenomenon secondary to varicella infection. While rapid recovery appeared to follow institution of cortisone therapy in the present case, the improvement noted may have been entirely coincidental. There was no reactivation of the disease process in this case.

Three roentgenograms.

JOHN P. FOTOPOULOS, M.D.
Northwestern University Medical School

Pneumopathies in Chronic Evolutive Polyarthrit. E. C. Bonard and H. Vasey. *Schweiz. med. Wchnschr.* 90: 866-870, Aug. 13, 1960. (In French) (Pompaples, Switzerland)

Among 50 cases of rheumatoid arthritis under survey for many years, pulmonary lesions were apparent radiologically in 18, and some respiratory disorder was found in 19 on clinical examination. While it is impossible at the present time to prove without biopsy that the radiological lesions are of true rheumatoid origin, it is thought, from experience and comparison with other collagen diseases and from the high incidence of abnormal findings in the lungs, that some relation must exist between the pneumopathies and the arthropathy.

Seven cases are reported. In Cases I and II there were no clinical manifestations of the pulmonary fibrosis demonstrated roentgenographically. There were clinical signs of pulmonary fibrosis in Cases III and IV, and in Case IV pulmonary infiltrates were also present.

Five roentgenograms; 4 tables.

Pulmonary Manifestations of Pancreatitis. David M. Roseman, O. Dhodanand Kowlessar, and Marvin H. Slesinger. *New England J. Med.* 263: 294-296, Aug. 11, 1960. (New York Hospital-Cornell Medical Center, New York, N. Y.)

A case of recurrent pancreatitis with mediastinal abscess, pulmonary infiltrates, and pleural effusion is reported. Multiple intra-abdominal abscesses communicating to the mediastinum were eventually found at operation.

Following their observation of this case, the authors reviewed 205 cases of proved pancreatitis seen at the New York Hospital over a thirteen-year period, with a total of 228 distinct clinical attacks. Pulmonary abnormalities were detected in the chest roentgenograms in 41 patients (20 per cent). Pleural effusion was observed in 15 cases and was usually left-sided, but was bilateral in 6 patients and exclusively right-sided in 1. In 20 patients there was elevation of the diaphragm, the left leaf in 9, the right leaf in 6, and both leaves in 5. Pleural reaction (including "adhesions" and "blunting of angle") occurred in 19 episodes, being left-sided in 11, right-sided in 3, and bilateral in 5 instances. Parenchymal infiltration was present in 16 cases, 5 in the right

lung, 8 in the left lung, and 3 on both sides. Disk atelectasis was found in 14 patients, occurring both unilaterally and bilaterally.

The importance of pulmonary signs in acute and chronic pancreatitis is stressed. The case reported illustrates the fact that the severity of the infectious involvement of the thoracic structures may obscure the diagnosis of the underlying pancreatitis.

Two roentgenograms.

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Experimental Pulmonary Edema. Karl-Eric Borgström, Ulla Ising, Erland Linder, and Anders Lunderquist. *Acta radiol.* 54: 97-119, August 1960. (University of Lund, Sweden)

Roentgen examination plays an important role in the diagnosis and differential diagnosis of pulmonary edema of different types. Especially in uremic patients is the recognition of pulmonary edema mandatory. Uremic pulmonary edema is characterized by central changes, surrounded by a free peripheral zone of normal lung parenchyma, 2 to 4 cm. in thickness and slightly broader at the lobe limits. The heart size is often normal.

Most authors claim that left heart failure is the essential etiologic factor in the development of the uremic pulmonary edema. Others feel that left heart insufficiency is secondary to the fluid retention in uremia. Several authors have suggested, as a cause of pulmonary edema, some toxic agent that could produce damage to the capillaries and thus alter permeability.

A theory is put forth by the present authors that the primary cause of pulmonary edema in uremia is damage by toxins on the bronchial vessel walls, causing permeability disturbances. By inducing an increased permeability in the bronchial circulation in dogs, it was found possible to produce changes in the lungs with the following roentgenologic characteristics: (1) central changes, with marked swelling of the bronchial walls and the walls of the pulmonary arterial and venous branches; (2) swelling of the esophageal and tracheal walls; (3) no involvement of the peripheral alveolar layers; (4) little or no pleural effusion; (5) no increase of heart size.

These findings are characteristic of the changes seen on roentgen examination of a patient with noncomplicated uremic pulmonary changes. This is in contrast to the "pulmonary capillary edema" and the lung changes in left heart failure, where edema fluid appears in the airways. The latter types of pulmonary change also differ in their peripheral location roentgenologically, when compared with the "bronchial capillary edema." The enlarged heart, in the condition of left heart failure, as well as the significant pleural effusion, are prominent findings on chest roentgenography. It has thus been possible to produce both "bronchial capillary edema" and "pulmonary capillary edema" simply by altering the permeability in the corresponding capillary regions.

The authors conclude from their present investigation that a change in the permeability of the bronchial capillaries may be the prime etiologic factor in the production of uremic pulmonary edema. Consequently, a reduction in the osmotic pressure of the blood produced by overhydration and/or a complicating left heart failure act as enhancing factors.

Twenty-six roentgenograms; 5 photomicrographs; 3 graphs.

PETER TORBEY, M.D.
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Neurogenic Tumors of the Mediastinum: A Clinicopathologic Study. Lewis S. Carey, F. Henry Ellis, Jr., C. Allen Good, and Lewis B. Woolner. *Am. J. Roentgenol.* **84**: 189-205, August 1960. (The Mayo Clinic, Rochester, Minn.)

Neurogenic tumors are the most common of the intrathoracic extrapulmonary tumors. They may be divided into two groups, depending on their origin: those that arise from nerve sheaths and those that arise from nerve cells. The nerve-sheath tumors (schwannomas or neurilemmomas) comprise the largest group; the vast majority are benign. The nerve cell tumors are thought to be true embryonic tumors, representing a proliferation of ganglion cells from undifferentiated elements that have migrated from the neural crest to form components of the paraganglionic autonomic nervous system; these tumors have been considered to be part of a continuous spectrum, ranging from the undifferentiated malignant neuroblastoma to the mature, benign ganglioneuroma. There also exists a small group of mediastinal neurogenic tumors, commonly referred to as "neurofibromas," that contain all the nerve elements.

The present paper deals with a study of 140 cases of extrapleural mediastinal tumors of neurogenic origin treated surgically at the Mayo Clinic over a period of thirty-three years, from 1923 through 1955. There were 86 benign schwannomas, 1 malignant schwannoma, 39 ganglioneuromas, 5 neuroblastomas, 5 plexiform neurofibromas, and 4 nonplexiform neurofibromas. The presenting complaints of patients with neurogenic tumors are mainly the result of pressure on neighboring structures. More than half of the schwannomas and ganglioneuromas were asymptomatic, and the tumor was first recognized on a routine roentgenogram of the thorax.

The roentgenograms or photographs of the roentgenograms in 94 of the cases of mediastinal neurogenic tumors were reviewed. These included 62 cases of schwannoma, 23 of ganglioneuroma, 4 of neuroblastoma, and 5 of neurofibroma. Three of the neurofibromas were plexiform in type and were associated with von Recklinghausen's disease. While it has been stated that neurogenic tumors do not have any characteristic roentgen features that would make it possible to distinguish one type from another, this is not altogether true. The schwannoma and the ganglioneuroma, when they occurred in the superior and inferior mediastinum, were often indistinguishable. In the postero-anterior view of the thorax each appeared as a dense, rounded, or oval circumscribed mass which blended with the mediastinal shadow medially but whose contour elsewhere was discernible from the mediastinal structures. In the lateral view, with some exceptions, the tumors were equally well defined, extending to the posterior limits of the intervertebral foramen (except in 3 cases in which the tumors arose from an unusual site such as the vagus or the recurrent laryngeal nerve). However, the appearance of ganglioneuromas that occurred in the region of the mediastinum posterior to the hilar structures, the base of the heart, and the root of the great vessels was usually characteristic, differing from that of all other neurogenic tumors. In the postero-anterior view the shadow cast by the ganglioneuroma in this region appeared as an elongated, flattened, or triangular density with the broad base toward the mediastinum. In many instances the shadow faded off superiorly or inferiorly, or both, so that the limits of the mass could not be discerned. In the lateral view the tumors were

characteristically poorly defined, and often there was only a suggestion of a density lying posteriorly, without a definite border.

In 1 of the 3 cases of plexiform neurofibroma associated with generalized neurofibromatosis, the tumor appeared as a flattened, somewhat lobulated mediastinal mass. The other 2 tumors presented as a double contoured ovoid density in the superior mediastinum. The roentgen appearance of 2 isolated mediastinal neurofibromas and the 1 malignant schwannoma was indistinguishable from that produced by the benign schwannoma.

One of the neuroblastomas appeared roentgenographically as a paramediastinal mass associated with an expanding destructive lesion involving the rib contiguous to the mass. The remaining 3 tumors appeared as ovoid masses which were indistinguishable from schwannomas.

Microscopic deposits of calcium were common within the ganglioneuroma, but were discernible roentgenographically in only 1 such case, where they were visualized as multiple small punctate densities. Calcium was seen in the roentgenograms of 7 patients with schwannoma; in 6 cases it was deposited in a strand-like or curvilinear fashion in the walls of large or moderately large cystic tumors.

Changes in the bones in association with neurogenic tumors were relatively common. Erosion of the ribs was seen in 39 cases and spreading of the vertebral ends of the ribs in 20 cases. Erosion of a pedicle was noted in 13 cases and erosion of a vertebral body in 7. Scoliosis occurred in 7 cases of ganglioneuroma and in 3 cases of schwannoma. Displacement of the mediastinal structures, particularly the trachea or esophagus or both, was observed in 15 cases of schwannoma and in 5 of ganglioneuroma.

All of the patients with neurogenic mediastinal tumor in the present series were treated surgically, with an operative mortality of 2.9 per cent. The results of follow-up are given.

The authors' studies disclosed no evidence to support the view that these tumors may undergo a process of maturation. Data on patients who underwent multiple operations or who died of a recurrent tumor indicate that none of the tumors changed their identity over the period concerned.

Seventeen roentgenograms; 7 photographs; 7 photomicrographs; 4 tables.

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Angiocardiography in the Differential Diagnosis of Pericardial and Mediastinal Tumors. Israel Steinberg. *Am. J. Roentgenol.* **84**: 409-423, September 1960. (525 East 68th St., New York 21, N. Y.)

The roentgen findings in 2 patients with intrapericardial tumors (a bronchogenic cyst and a teratocarcinoma with pericardial effusion) are contrasted with those in 2 patients with mediastinal tumors (a dermoid cyst and a thymic hyperplasia).

In mediastinal tumors, valuable clues are obtained by roentgen positioning and the demonstration of separation of the components of the cardiac silhouette. Angiocardiography, however, provides the best evidence of the extracardiac nature of the mass.

In intrapericardial masses, conventional roentgenography is of very little aid in diagnosis, whereas angiocardigrams may show the characteristic rotation of

the heart by the intrapericardiac mass, as well as demonstrating pericardial effusion.

The exclusion of heart disease by angiocardiology, when there is a massive cardiac silhouette, will hasten surgical exploration of the mediastinum and pericardium. Thus, serious complications such as cardiac tamponade and pericardial and mediastinal infection may be avoided.

Forty roentgenograms; 8 photographs; 2 photomicrographs.

JOSEPH P. TOMSULA, M.D.
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Localized Mediastinal Lymph Node Hyperplasia. Report of a Case with Roentgen Findings Simulating Posterior Mediastinal Neurofibroma. Isadore Katz and Roman Dziadziw. *Am. J. Roentgenol.* **84**: 206-212, August 1960. (450 Clarkson Ave., Brooklyn 3, N. Y.)

Benign localized mediastinal lymph node hyperplasia was first described by Castleman in 1954 (*New England J. Med.* **250**: 26, 1954). The authors report a case to call attention to this entity, which should be considered in the differential diagnosis of tumors located not only in the anterior or middle compartments of the mediastinum but in the posterior compartment as well. The roentgen features of lymph node hyperplasia, and of posterior mediastinal masses in general, are discussed.

The condition is regarded as a response to a chronic inflammatory process of long standing. Microscopically, there is hyperplasia of the lymphoid follicles and marked capillary proliferation with endothelial hyperplasia. There seem to be no definite clinical symptoms, and almost all of the cases which have been reported were discovered during routine periodic or mass survey examinations. On the roentgenogram the hyperplastic lymphoid structures appear in the mediastinum as discrete, sharply circumscribed hilar masses resembling lymph node enlargements, parenchymal lung masses, or dilated vessels. In a few cases, they have appeared as multilobulated anterior mediastinal masses resembling lymphomatous, thyroid, thymic, or teratomatous tumors. At the operating table some have been mistaken for thymomas and others for bronchial adenomas. None have shown calcification roentgenographically or histologically.

The authors' patient was a 33-year-old white man who was admitted to the hospital for treatment of a mass discovered on a chest survey roentgenogram. This was spherical in contour and measured 5.5 cm. in diameter. It was situated in the right paravertebral gutter and had produced slight erosion and pressure sclerosis of the inferior margin of the vertebral ends of the right fourth and fifth ribs. The roentgen findings were considered typical of neurofibroma or other neoplasm of neurogenic origin. A roentgenogram taken nine years earlier showed the same mass, which at that time measured only 3.5 cm. in diameter. The preoperative and postoperative surgical diagnoses were "probable neurofibroma." Only on histologic section was the true diagnosis apparent. This showed an enlarged lymph node with compressed germinal centers in the stroma and a large aggregate of typical lymphocytes throughout.

Examples are recorded of lesions of the paravertebral gutter, originally thought to be of neurogenic origin, but later proved to be due to other causes.

Four roentgenograms; 2 photomicrographs.

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THE BREAST

Xeroradiography of the Breast. Howard R. Gould, Francis F. Ruzicka, Jr., Rafael Sanchez-Ubeda, and Joseph Perez. *Am. J. Roentgenol.* **84**: 220-223, August 1960. (St. Vincent's Hospital of the City of New York, New York 11, N. Y.)

In xeroradiography, a selenium-coated and charged metal plate is used instead of a film. Roentgen rays, according to their intensity, cause a varying run-off of charge on the area of the plate which they strike. After exposure, the plate is dusted with charged calcium carbonate powder, and an image similar to that seen on conventional roentgenographic film is produced. The image may be preserved by transferring it to paper by an adhesive technic or by photographing it. Because the resolving power of the xeroradiographic plate is greater than that of conventional film, greater image detail is achieved.

Xeroradiography was employed in 13 patients with normal breasts to determine whether the procedure has advantages over conventional roentgenography. The parenchymal structures were found to be more easily identified when outlined by the greater fatty content of the breast with increasing age. Even in the younger patients, the ducts and trabeculae were well seen. The chest wall itself was also clearly demarcated. Vessels coursing in the subcutaneous tissues stood out distinctly from the breast parenchyma itself. On several xeroradiographs, the reticular appearance of the subcutaneous fat was visible. Xeroradiographs of one postpartum breast revealed dilated edematous ducts and trabeculae; conventional soft-tissue roentgenography in this type of breast will often show an almost homogeneous density.

The authors believe that xeroradiography deserves further trial in the evaluation of breast lesions, especially in those that are adjacent to the chest wall, where detail is apt to be poor with conventional roentgenography.

Three xeroradiographs; 1 drawing.

JOHN W. WILSON, M.D.
Johnstown, Penna.

THE HEART AND BLOOD VESSELS

The Angiocardigraphic Diagnosis of Ventricular Septal Defect. A. Castellanos, Otto Garcia, Eloina Gonzalez, Raul Pereiras, and H. Mercado. *Am. J. Roentgenol.* **84**: 424-435, September 1960. (23 No. 1, 107, Vedado, Habana, Cuba)

The authors review their own earlier efforts and those of others in the diagnosis of ventricular septal defect. For a suggestive diagnosis several signs should be present: (1) blurred appearance of the infundibulum in the dextrocardiogram; (2) enlargement of the left auricle; (3) dilatation of the pulmonary artery and its branches; and (4) reopacification of the main pulmonary artery and its branches. Until now, angiocardiology has been of limited value, since only the indirect signs enumerated above have been noted. For a positive or direct diagnosis of ventricular defect, it is necessary actually to see the stream or jet of blood spurting through the defect from the right ventricle into the left ventricle or inversely. Cineroentgenography permits a clear image of the radiopaque medium as it emerges from the septal defect. Thirty cases were studied by the authors by this means. Their own conclusions are

the best summation of their extensive and thorough observations.

"1. The left anterior oblique projection is best suited for direct diagnosis of ventricular septal defect, isolated or associated with other lesions with a shunt from left to right; it permits visualization of the jet of blood spurting from the left ventricle into the right ventricle through the septal defect during ventricular systole.

"2. Peripheral intravenous injection can be useful if the following requirements are met: (a) high concentration of radiopaque substance; (b) sufficient quantity; and (c) very rapid injection.

"3. The method which demonstrates the roentgen characteristics best is the intracardiac or selective method, in which the injection is made into the left auricle or the left ventricle itself. If an adequate quantity of radiopaque material is injected rapidly, the contrast of the left cardiac chambers is very intense and permits small jets of blood to be visualized in the left anterior oblique projection, even when the central roentgen-ray beam is not parallel to the ventricular septum. The advantages of this method are that the location of defect, its diameter, the number of defects present, and the direction of the spurting blood can be ascertained.

"4. An ultra-fast cassette or film changer, 8 or 12 views per second, offers many chances of visualizing the jet; with a slow seriograph of 2 views per second, the chances are rather limited.

"5. The best technique is to use cineangiocardiology (cinefluorography). The standard equipment exposes about 60 frames per second. When the injection is made via the peripheral veins with a good technique, even without the proper left anterior oblique projection, the jet of blood may be visualized in many cases.

"6. Intracavitary or selective injection with cinefluorography is the ideal method for the diagnosis of ventricular septal defects, either isolated or associated with other cardiac anomalies."

Sixty roentgenograms; 1 diagram.

JOSEPH P. TOMSULA, M.D.
Baton Rouge, La.

Ventricular Septal Defect with Patent Ductus Arteriosus. A Clinical and Hemodynamic Study. Arthur A. Sasahara, Alexander S. Nadas, Abraham M. Rudolph, Martin H. Wittenborg, and Robert E. Gross. *Circulation* 22: 254-264, August 1960. (Children's Medical Center, Boston 15, Mass.)

Within the past few years, the authors have seen 22 patients with combined ventricular septal defect and patent ductus arteriosus, proved at cardiac catheterization. The clinical and hemodynamic features of these cases are described and the therapeutic implications of this combination of anomalies are discussed.

The striking findings on physical examination were gross undernourishment and a wide pulse pressure in the great majority of the patients. Almost all had harsh systolic murmurs along the mid left sternal border and only 2 had continuous Gibson murmurs. The electrocardiogram is of minor importance in the diagnosis of this combination of lesions. All patients showed roentgen evidence of cardiac enlargement, which was mild to moderate in 9 and severe in the others. The enlargement involved both ventricles (the left usually predominating) in 17 cases, whereas 2 showed pure right and 3 pure left ventricular enlargement.

Left atrial enlargement could be demonstrated in 19 patients. The main pulmonary artery segment was prominent, often markedly so, in 16. Active pulmonary vascular engorgement was thought to be present in all patients, but expansile pulsations of the intrapulmonary vessels or "hilar dance" were observed in only 6 of these. With the exception of infants in cardiac failure, the amplitude of pulsation of the left ventricle on fluoroscopy was increased. Similarly, the main pulmonary artery segment frequently showed a hyperactive beat, characterized by increased amplitude of pulsations, and in most patients the aorta shared in this hyperactivity. Fluoroscopically, then, there appeared to be no definite pattern to differentiate these cases from those with an uncomplicated ventricular septal defect or patent ductus arteriosus.

Careful hemodynamic studies are crucial in the diagnosis of these two lesions. At the ductal level passage of the catheter establishes the diagnosis, or an increase in oxygen saturation greater than 5 per cent in comparison to the right ventricular blood strongly suggests the presence of a patent ductus arteriosus. The great majority of the ventricular septal defects were diagnosed by an increase in the oxygen saturation of 10 per cent or greater at the ventricular level. Almost all of the patients had pulmonary artery hypertension.

Attempts at surgical correction of these defects were undertaken in 13 patients. Division or ligation of the ductus was the only procedure performed in 9; in the other 4 both defects were closed. In 3 of the latter group the ductus was an incidental finding during surgery for correction of the septal defect. In the first group of 9 patients, 2 died and 2 improved significantly. Two patients in the second group died and 2 showed marked improvement. Nine patients were treated medically; all were alive at the time of writing.

It is suggested that if the patent ductus arteriosus is diagnosed on the basis of a typical machinery murmur, correction of this lesion is indicated, irrespective of the associated ventricular defect. If the clinical picture is suggestive of a ventricular defect alone and the combination of lesions is discovered only at catheterization, then simultaneous correction of the two lesions is recommended. In small infants in whom the combined operation is difficult, trial of medical management is advised; only if this fails to accomplish the expected result should division of the ductus be undertaken.

Seven roentgenograms; 1 phonocardiogram; 5 tables.

ZAC F. ENDRESS, M.D.
Bloomfield Hills, Mich.

Left Cardiac Ventriculography by Means of Percutaneous Catheterization of a Femoral Artery in the Diagnosis of Mitral Insufficiency. G. Tori and G. F. Garusi. *Acta radiol.* 54: 170-176, September 1960. (University of Bologna, Italy)

The authors have found left cardiac ventriculography by means of percutaneous catheterization of a femoral artery an accurate method for the preoperative assessment of the presence (or absence) and degree of mitral regurgitation. They base their conclusions on a series of 20 cases of mitral disease examined by this technique. More than half of the patients had pure mitral stenosis without any degree of regurgitation into the left atrium; the findings were confirmed at operation.

It appears from a comparison with other procedures that left cardiac ventriculography after percutaneous catheterization of a femoral artery is the simplest to

perform and is practically free from risks and contraindications. Serial films must be obtained over a sufficiently long period to show the contrast medium while it persists in the left ventricle and thus record the behavior of the reflux in more than one heart cycle. This is to avoid the possibility of transitory mitral regurgitations, which admittedly may occur and lead to errors in diagnosis. For the same reason, simultaneous electrocardiography is advisable for recording disturbances in rhythm. Any significant degree of regurgitation into the left atrium during the procedure is considered pathognomonic of mitral valve insufficiency.

Two roentgenograms. THEODORE E. KEATS, M.D.
University of Missouri

Calcification of the Inner Wall of the Atrium in Mitral Stenosis. Z. Svoboda and M. Sobotková. *Fortschr. a. d. Geb. d. Röntgenstrahlen* 93: 163-166, August 1960. (In German) (Krankenhaus Bulovka, Prague, Czechoslovakia)

Calcification of the cardiac valves, an annulus fibrosus, and of the coronary arteries frequently occurs. Less common are pericardial, endocardial, and myocardial calcifications. Calcifications of a mural thrombus and of cardiac neoplasms are rare.

The case is reported of a woman, aged 52, with a history of rheumatic heart disease of thirty years duration. The patient suffered from exertional dyspnea, cyanosis, hemoptysis, and other manifestations of decompensation. Heart and liver were enlarged, and there was edema of the legs and abdominal wall. Roentgenograms revealed advanced mitral stenosis and a pulmonary infarct at the right base, with associated pleural effusion. Of special interest was a rather thick calcium ring in the area of the left atrium, measuring 9 cm. in width and 6 cm. in height.

Autopsy disclosed calcification of the left atrial wall and of a contiguous mural thrombus.

Four roentgenograms; 1 photograph.

ERNEST KRAFT, M.D.
Northport, N. Y.

Transposition of the Great Arteries. A Correlation of Clinical, Physiologic and Autopsy Data. Jacqueline A. Noonan, Alexander S. Nadas, Abraham M. Rudolph, and G. B. C. Harris. *New England J. Med.* 263: 592-596, Sept. 22; 637-642, Sept. 29; 684-692, Oct. 6; 739-744, Oct. 13, 1960. (Children's Hospital Medical Center, Boston 15, Mass.)

Transposition of the great vessels is one of the most serious of cardiac anomalies. In one autopsy series it was found to account for 7.4 per cent of cases of congenital heart disease. The present publication reviews the clinical features, physiologic data, and natural history of 50 proved cases, all of which were studied by cardiac catheterization. The age of the patient at the time of investigation ranged from eleven days to eleven years. Twenty were over two years old.

Prominent physical findings among the group studied were cyanosis, clubbing, varicosities of extremities and scalp, chest deformities, and large square heads. Growth and development were delayed in the surviving infants. Additional noncardiovascular congenital anomalies were rare. Dyspnea was present at rest in most patients and increased or became obvious with exertion in all. A history of congestive heart failure was obtained in the great majority.

For comparative purposes the following classification was adopted by the authors:

Group 1. Intact ventricular septum

Group 2. Defect of ventricular septum

A. With pulmonary stenosis

B. With pulmonary vascular obstruction

C. With large pulmonary blood flow

The clinical picture was thought to be of little value in differentiating the four groups. However, congestive failure developing in the first few months of life suggests Group 1. Absence of congestive failure suggests Group 2 A. Mild cyanosis was most common in Group 2 C.

Of routine laboratory studies, urinalysis was unremarkable, and the physiologic anemia normally noted by two months of age did not occur. A mild anemia which responded to iron therapy developed between six and twenty-four months of age in some infants.

Electrocardiograms were of some value in differentiating the four groups. Right-axis deviation, hypertrophy of the right ventricle, and P pulmonale constituted the most common picture, but patients in Group 2 C usually had normal axes or left-axis deviation, with hypertrophy of both ventricles or of the left ventricle alone. Partial reversal of the R/S progression or an adult progression suggests the presence of an associated ventricular defect, since all patients in Group 1 had a complete reversal.

Chest roentgenograms were suggestive of transposition of the great vessels but not diagnostic. A narrow waist and "egg shaped" heart suggests Group 1. A normal or prominent main pulmonary artery suggests Group 2 B or 2 C, and a normal heart size and pulmonary vasculature, Group 2 A. A negative chest roentgenogram does not necessarily exclude the diagnosis of transposition.

Cardiac catheterization and angiocardiology were very important in establishing a diagnosis. If the pulmonary artery was entered by the catheter and was found to have a higher oxygen saturation than the systemic artery or if angiocardiology showed the pulmonary artery to arise exclusively from the left ventricle a diagnosis of transposition of the great vessels was considered proved.

The authors believe that reliance is to be placed chiefly on cardiac catheterization for an understanding of the complete hemodynamics of transposition of the great arteries in most patients. Angiocardiology is of value in tracing the position and course of the vessels but does not give information regarding the level and direction of intracardiac shunts and the pressures and flows in the pulmonary and systemic circulations.

Medical measures in these cases were necessarily limited and treatment was generally symptomatic.

Surgical management was concerned with the development of various shunting procedures. Only 2 of 12 patients in the present series subjected to operation survived. This is believed to be due in part to poor selection. Briefly the indications for surgery are as follows:

Patients in Group 2 A, unless severely anoxic, should not be operated upon since the chances of survival are relatively good without surgery. Any patient in Groups 1 or 2 C who is not doing well should be offered surgery since the prognosis without it is poor. Although patients in Group 2 B do not live as long as the

majority in Group 2 A, survival beyond five years of age is not uncommon. Therefore, until surgical mortality rates decline, surgery should be withheld from this group as long as possible.

Twenty-five of the 50 cases reviewed here had terminated fatally, and autopsy was obtained in 21. The findings are tabulated.

Seventeen figures; 17 tables.

JOSEPH M. BEHUN, M.D.
Mercy Hospital, Pittsburgh, Penna.

Total Anomalous Pulmonary Venous Return Below the Diaphragm. The Roentgen Appearances in Three Patients Diagnosed During Life. G. B. C. Harris, E. B. D. Neuhauser, and Andres Giedion. *Am. J. Roentgenol.* 84: 436-441, September 1960. (Children's Hospital Medical Center, Boston 15, Mass.)

The roentgen appearance of total anomalous pulmonary venous drainage into a persistent left superior vena cava is well known. The roentgen features of total anomalous pulmonary venous return below the diaphragm, however, seem to be less familiar. Although no patient with this form of pulmonary venous drainage has survived beyond the age of three months, the lesion might well lend itself to surgical correction and prompt diagnosis may prove to be of more than academic interest.

Seven infants with total anomalous pulmonary venous return below the diaphragm have been seen in the Children's Medical Center (Boston, Mass.) in the past seven years. Four of these cases have been reported previously (Guntheroth *et al.* *Circulation* 18: 117, 1958. *Abst. in Radiology* 72: 783, 1959). The authors present the last 3 cases and discuss the roentgen findings which led to the diagnosis. In each case the pulmonary venous anomaly was accompanied by a patent foramen ovale or atrial septal defect with or without an associated patent ductus arteriosus. Roentgen examination of the chest showed the heart to be within normal limits in size and configuration. The interstitial supporting tissues of the lungs were thickened and had hazy margins with an appearance quite suggestive of congestion and edema. It is the apparent discrepancy of a heart of normal size in a cyanotic newborn infant with both clinical and roentgen signs of congestive heart failure which permits the correct diagnosis to be entertained. Cardiac catheterization studies and angiocardiography can confirm the diagnosis.

[Four cases of infradiaphragmatic pulmonary venous drainage are reported by Levin and White in *Radiology* 76: 894, June 1961.—Ed.]

Five roentgenograms.

JOSEPH P. TOMSULA, M.D.
Baton Rouge, La.

Varicosities in the Lingular Branch of the Pulmonary Vein. H. Hagen and K. Heinz. *Fortschr. a. d. Geb. d. Röntgenstrahlen* 93: 151-159, August 1960. (In German) (I. Medizinische Klinik der Stadt. Krankenanstalten Wilhelmshaven, Germany)

Varicose veins, as well as arterial and arteriovenous aneurysms, are rare vascular manifestations in the lungs. They cannot be differentiated from one another on ordinary roentgenograms of the chest.

Pulmonary varices are especially rare. Cyanosis and clubbing of fingers are absent in this condition because arteriovenous communications are lacking. An intrapulmonary round focus is the outstanding roentgeno-

logic finding. It has to be differentiated from tuberculosis, primary and metastatic neoplasm, echinococcus cyst, bronchopneumonia, and peribronchitis. Pulmonary infiltration can be simulated when surrounding lung tissue is compressed or invaded by hemorrhage from a ruptured varix. The vascular nature of the lesion can be confirmed by various views, especially oblique and lateral tomograms. These will show a band-like connection with hilar structures. The shadow undergoes no variation in size with the Valsalva and Müller maneuvers, in contradistinction to arteriovenous aneurysms. Only 7 cases are said to have been recognized during life.

The case reported here is believed to be the first of a varix of the lingular branch of the pulmonary vein to be diagnosed antemortem. The patient was a locksmith, aged 58. A round focus was noted in the lingula of the left upper lobe, measuring 23 × 32 mm. For three years, it had been treated medically without result. Fluoroscopic study failed to disclose any pulsation. There was a band-like connection between the focus and hilar structures, best seen on lateral tomograms. Segmental resection of the lingula revealed marked distention of pulmonary veins with compression atelectasis of surrounding lung tissues.

Seven roentgenograms; one photomicrograph.
ERNEST KRAFT, M.D.
Northport, N. Y.

Spinal Cord Injury as a Complication of Aortography. Duncan A. Killen and John H. Foster. *Ann. Surg.* 152: 211-230, August 1960. (Vanderbilt University School of Medicine, Nashville, Tenn.)

From a review of the literature and a card survey of the Chiefs of Radiology and Urology in the United States, the authors collected 38 cases of spinal cord injury during aortography. For 28 of these, detailed information was obtained. Nineteen patients (70 per cent) had complete paralysis of both legs; 5 (31 per cent) had complete loss of sensation of the hindparts. There was loss of urethral and anal sphincter control in 18 (90 per cent). Of 22 patients with neurologic follow-up, 9 had permanent spastic paraplegia, 8 weakness of varying degree; 5 had recovered completely.

Pathologic examination of the spinal cord was carried out in 6 cases. In the early post-injury period the cord was swollen, pale, and soft. In the older lesions there were degenerative changes in the gray matter of the mid-thoracic or more caudad regions of the spinal cord, ranging from pigmentary changes in the ventral horn neurons to liquefactive necrosis of the entire gray matter. In no instance was there evidence of thrombosis of the anterior spinal artery or of the intercostal and lumbar arteries at their points of origin from the aorta.

General anesthesia was used in 15 cases (79 per cent), and a barbiturate compound was employed solely or in combination with another anesthetic agent in 12 of these.

In 2 patients aortography had been performed before (four weeks previously in 1 and nineteen and six days previously in the other). Urokon (sodium acetrizate) was employed in 21 instances (84 per cent), Diodrast twice, and Neo-Iopax and sodium iodide once each. In the only case in which Hypaque was used, Urokon was also injected. The total amount of contrast medium used was 40 ml. or more in 41 per cent of the cases. The injection was repeated in 11 cases.

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The mechanism of spinal cord injury during aortography and the factors which predispose to it are discussed. The authors believe that the injury is most likely a direct toxic effect of the contrast medium upon the nerve cells of the spinal cord. They suggest the following safeguards, in order of importance:

1. Employment of the *least toxic agent* of adequate contrast (thought currently to be Hypaque 50 per cent to 90 per cent).
2. Use of a *single injection* of contrast material.
3. *Prone positioning* of the patient, if feasible, during aortography.
4. Use of the *smallest volume* of contrast medium which will permit adequate roentgenologic delineation of the structures to be visualized.
5. Avoidance of *barbiturate anesthesia*.

Two roentgenograms; 2 drawings; 12 tables.

ZAC F. ENDRESS, M.D.
Bloomfield Hills, Mich.

Significance of Repeat Injection of Contrast Medium in the Genesis of Kidney and Spinal Cord Damage Resulting from Abdominal Aortography.

Duncan A. Killen and Edward M. Lance. *Ann. Surg.* 152: 231-239, August 1960. (Vanderbilt University School of Medicine, Nashville, Tenn.)

Although a direct relationship between tissue toxicity and the chemical structure of the angiographic contrast agents has been established, the use of repeated or multiple injections of the medium during the performance of aortography has been implicated as a factor in the causation of renal and spinal cord damage (see preceding abstract). The three least toxic of the organic iodide contrast agents were investigated in relation to this problem. Diodrast 70 per cent, Miokon 90 per cent, and Hypaque 90 per cent were tested as to their toxic effect upon the kidney and spinal cord when each substance was injected singly and again after an interval of fifteen minutes into the abdominal aorta of healthy, adult mongrel dogs.

Repeat aortic injection of Diodrast or Miokon increased the incidence of azotemia secondary to renal damage if it was performed within fifteen minutes following the primary injection. Although no evidence was obtained from the present study that the same statement is true with regard to Hypaque, a more strenuous test of renal tolerance to this substance would perhaps reveal such a deleterious effect as the consequence of repeat injections.

Repeat aortic injection of any of the three media increased the incidence and severity of spinal cord injury if given within an interval of fifteen minutes following the primary injection.

The toxicity of the aortographic contrast agents tested in this study vary: Diodrast is most toxic to renal tissue, while Miokon possesses the greatest neurotoxic potential. Hypaque exhibits the lowest nephrotoxicity and the lowest neurotoxicity.

Ten graphs; 4 tables. ZAC F. ENDRESS, M.D.
Bloomfield Hills, Mich.

Arteriovenous Fistulas of Coronary Arteries. W. Postmann and W. Geissler. *Fortschr. a. d. Geb. d. Röntgenstrahlen* 93: 143-150, August 1960. (In German) (I. Medizinische Universitätsklinik der Charité, Berlin, Germany)

Congenital arteriovenous fistulas of the coronary vessels are rare; only 40 cases could be found in the

literature. The shunt occurs not only between arteries and veins, but even more frequently between arteries and a heart chamber.

On auscultation, one hears a machinery-like murmur which suggests the following possibilities: (1) patent ductus arteriosus with insufficiency of the pulmonic valve; (2) aneurysm of the sinus of Valsalva perforating into the right atrium or ventricle; (3) ventricular septal defect with aortic insufficiency; (4) anomalous drainage of pulmonary veins into the left brachiocephalic vein; (5) aortopulmonary fistula.

With increased use of percutaneous retrograde aortography and coronary arteriography, fistulas are now expected to be discovered more frequently. Of clinical significance is the size of the shunt. There is always danger of aneurysmal dilatation of the afferent vessels, resulting in thrombosis, subacute bacterial endocarditis, and myocardial ischemia. Rupture of a vessel is unlikely, but ligation is nevertheless helpful to alleviate cardiac symptoms.

A single case is reported. The patient was an electrical engineer, aged 41, with symptoms of fatigue, dizziness, headaches, exertional dyspnea, and angina pectoris. There was a machinery-like murmur in the left parasternal area, especially on expiration. Roentgenograms of the chest revealed slight enlargement of the left ventricle and stenosis of the aortic isthmus, as well as dilatation of the left subclavian artery. Coronary arteriography disclosed aneurysmal widening of the right coronary artery with drainage into dilated veins. The diagnosis was arteriovenous fistula of the right coronary artery with typical widening of the afferent limb and aneurysm at the junction with the veins of the right heart. The pathologic changes are well illustrated.

Four roentgenograms; 2 tables; 2 electrocardiograms. ERNEST KRAFT, M.D.

Northport, N. Y.

Simultaneous Occurrence of Intracranial Aneurysm and Arteriovenous Malformation. Report of Case Successfully Treated. Ronald Fine, Alastair Paterson, Leslie Steven, and J. B. Gaylor. *Brit. M. J.* 2: 711-712, Sept. 3, 1960. (Western Infirmary, Glasgow, Scotland)

A case is reported of an aneurysm of the right posterior inferior cerebellar artery and an arteriovenous malformation supplied by branches from the superior cerebellar artery and the posterior inferior cerebellar artery. Both lesions were demonstrated by vertebral angiography, and both were successfully treated, with uneventful recovery save for residual ocular signs. It is suggested that the coexistence of intracranial aneurysms and cerebral angiomas will become more obvious with the wider application of complete arteriography in subarachnoid hemorrhage.

Three roentgenograms.

Diagnosis of Aneurysms of the Hepatic and Splenic Arteries by Intravenous Abdominal Aortography. Israel Steinberg. *New England J. Med.* 263: 341-343, Aug. 18, 1960. (New York Hospital-Cornell Medical Center, New York, N. Y.)

A safe and practical method of visualizing the abdominal aorta and its branches by simultaneous intravenous injection of concentrated contrast material into both arms has been reported (Steinberg, I., *et al.*: *Am. J. Roentgenol.* 82: 758, 1959. *Abst. in Radiology*

75: 494, 1960). The circulation time is predetermined by a preliminary injection of 3 ml. of sodium dehydrocholate (Decholin). Experience in over 250 cases indicates that adding half a second to the predetermined circulation time and making a two-second exposure will regularly visualize the abdominal aorta. Reactions to the contrast material (average dose, 1 ml. per kilogram of body weight) have been mild and transient.

Two cases are reported—one of arteriosclerotic hepatic-artery aneurysm in a 72-year-old man and the other of arteriosclerotic splenic-artery aneurysm in a 67-year-old woman. In both patients the arteriosclerotic lesions were visualized by the method of intravenous abdominal aortography. Both patients were asymptomatic. The splenic-artery aneurysm was excised to preclude rupture. Surgery was not advised in the 72-year-old man with the hepatic-artery aneurysm because it had not caused symptoms in a four-year period of observation.

An increasing number of reports of the successful removal of hepatic-artery aneurysms, however, indicate that repair of such lesions is feasible and the risk less than that of rupture. Intravenous abdominal aortography permits diagnosis of abdominal aneurysms without the complications of translumbar aortography. Accordingly, the author predicts that more and more abdominal aortic, splenic, and hepatic aneurysms will be discovered before rupture and at a time when they are amenable to curative treatment.

Two roentgenograms.

MORTIMER R. CAMIEL, M.D.
Brooklyn, N. Y.

Dilated Azygos Vein Simulating a Mediastinal Tumor. Report of a Case. Melchor H. Magbitang, Franklin C. Hayford, and James M. Blake. *New England J. Med.* 263: 598-600, Sept. 22, 1960. (F. C. H., Glenridge Hospital, Schenectady, N. Y.)

Radiographic examination of the chest of a 35-year-old woman with gynecologic complaints incidentally revealed a mediastinal tumor on the right side extending far out in the superior mediastinum. Bronchoscopy showed a slight bulging of the posterior tracheal wall at approximately the 20-cm. level. In view of an elevated total protein and serum globulin, a diagnosis of Boeck's sarcoid was entertained. An exploratory thoracotomy disclosed an azygos vein in normal location but approximately ten times its normal size. Its course was normal and it entered the superior vena cava at the usual site. The superior and inferior venae cavae were both smaller than normal, particularly the inferior vena cava. No other abnormalities were detected within the chest.

In the presence of a faulty development of the inferior vena cava, the azygos vein may represent a principal channel of venous return from the lower parts of the body. Malformation of this type has been described as aplasia or hypoplasia of the inferior vena cava, with azygos drainage, and has been suggested as the probable cause of idiopathic dilatation of the azygos vein. Other causes of azygos-vein dilatation include right-sided heart failure, obstruction of the superior and inferior venae cavae, and portal vein hypertension.

Dilatation of the azygos vein should always be taken into consideration in the diagnosis of mediastinal shadows, especially when they extend to the right. It is suggested that the following studies be performed in such cases. A roentgenogram should be taken with the patient in the supine or Trendelenburg position to demonstrate the dilated vein better. Good results have

been obtained with increased penetration and oblique views. The Valsalva and Müller maneuvers should be employed; the dilated azygos vein decreases in size with the Valsalva maneuver and increases with the Müller. This is hard to demonstrate, however, in a patient with heart failure. Angiocardiography and intraosseous phlebography have helped in some cases. Contrast medium injected into the spinous process of the eleventh thoracic vertebra leads to extensive filling of the vertebral venous plexus and opacification of the dilated azygos arch.

One roentgenogram. ZOLTAN SZALONTAY, M.D.
Mercy Hospital, Pittsburgh, Penna.

A Case of Capillary Haemangioma with Some Observations on Angiography and Microangiography. J. A. Veiga Pires. *Brit. J. Radiol.* 33: 491-495, August 1960. (Royal Northern Hospital, Holloway London, N. 7, England)

The case is reported of a woman who had a histologically confirmed capillary hemangioma, or nevus flammeus, on the tip of the right index finger. Arteriography was carried out in the hope of demonstrating vascular changes and the extent of the lesion, but no pathological vessels or alterations in the main feeding vessels were disclosed. The reasons for this failure appear to lie in the limitations of the routine angiographic technique, which fails to demonstrate the richness of the microscopic meta-arteriolar and capillary plexuses of the skin of the pulp of the fingers. Microradiographs showing the normal vascular pattern of injected skin of pulp of finger and of dorsum of hand are reproduced.

The author postulates that there must be a critical phase or size at which early changes in the caliber and number of the main feeding vessels of the lesion may be appreciated or, as in the case of Bartley and Wickham (*Acta radiol.* 51: 81, 1959. *Abst. in Radiology* 73: 945, 1959), at which small vascular lakes become obvious. To study this type of lesion there seems to be a need for angiographic and radiological techniques directed toward demonstrating arteriolar and capillary filling in peripheral angiography.

Six roentgenograms; 1 photomicrograph.

Costal Intraosseous Venography in Portal Hypertension. Robert Schobinger, Philip Cooper, Louis M. Rousselot, and Joseph Stein. *Arch. Surg.* 81: 143-150, July 1960. (VA Hospital, Bronx 68, N. Y.)

The material contained in this article was presented as a scientific exhibit at the 108th Annual Meeting of the American Medical Association, June 8-12, 1959, to show the value of costal intraosseous venography in diagnosis of portal hypertension. The technique is described and illustrative roentgenograms are reproduced.

THE DIGESTIVE SYSTEM

Recognition and Treatment of Esophageal Perforations. Donald L. Paulson, Robert R. Shaw, and John L. Kee. *Ann. Surg.* 152: 13-21, July 1960. (3810 Swiss Ave., Dallas 4, Texas)

Perforations of the esophagus may be due to trauma, either direct or indirect, an inflammatory lesion, or neoplasm. The most frequent use of endoscopic procedures in recent years in the diagnosis and treatment of diseases of the esophagus has been accompanied by a pronounced increase in the incidence of esophageal perforations. Since the mortality of untreated perfora-

tions is 70 per cent or more, early diagnosis and treatment are of utmost importance. The recognition of esophageal perforation depends on an alertness to the significance of severe pain, dysphagia, fever, and elevated pulse rate, together with the presence of air or fluid in the neck, mediastinum, or pleura, following the ingestion of a foreign body, instrumentation of the esophagus, vigorous vomiting, trauma to the neck or chest, or associated intrinsic disease of the esophagus. Roentgen studies are imperative for an accurate diagnosis. Plain films of the neck or thorax are usually sufficient for this purpose, though sometimes in a doubtful case examination of the esophagus with radiopaque liquids may be of assistance in localizing the perforation. The most important roentgen signs in the cervical region are evidence of gas in the tissues, widening of the retrovisceral space, broadening of the superior mediastinum, and anterior or lateral displacement of the trachea. In the thoracic perforations, mediastinal widening, air in the mediastinum or neck, fluid levels in the mediastinum, pleural fluid or pneumothorax are seen singly or in combination.

Closure of the esophageal perforation, even late after infection of surrounding tissues has occurred, together with drainage, antimicrobial drugs and general supportive therapy, results in a low mortality, healing, and a low morbidity. The authors' experience with 23 patients with esophageal perforations is tabulated; in this group the mortality rate was 18 per cent.

Sixteen roentgenograms; 2 tables.

RICHARD H. GREENSPAN, M.D.
New Haven, Conn.

Intramural Diverticulosis of the Oesophagus and Rokitansky-Aschoff Sinuses in the Gall-Bladder.

Karl Mendl, J. M. McKay, and Clive H. Tanner. *Brit. J. Radiol.* 33: 496-501, August 1960. (Morriston Hospital, Swansea, Wales)

The authors report 2 cases, each the first of its kind to be published: (1) intramural diverticulosis of the esophagus and (2) Rokitansky-Aschoff sinuses demonstrated by filling the gallbladder through a cholecystoduodenal anastomosis during a barium-meal examination.

The first patient was a 56-year-old man who complained that large pieces of solid food would stick behind the sternum. On bending forward, the food would go down, with immediate relief of pain. Esophagoscopy was normal. A barium swallow revealed innumerable contrast shadows, the size of a pin-head, along the whole length of the esophagus, parallel to and 2 mm. outside its smoothly outlined lumen. Most of these shadows connected with the lumen by narrow ducts. This appearance is considered analogous to the radiographic image of Rokitansky-Aschoff sinuses in the gallbladder and is believed to represent intramural narrow-necked diverticula. The cystic dilations of the blind ends suggest that they are pulsion diverticula due to increased intraluminal pressure.

The second patient was a 62-year-old woman with obstructive jaundice. A cholecystoduodenostomy was performed; histologic examination of the specimen revealed adenocarcinoma of the ampulla of Vater. Nineteen months following surgery, an upper gastrointestinal series showed barium filling the gallbladder through an anastomosis between its fundus and the descending portion of the duodenum. The radiographic appearance was pathognomonic of intramural

diverticulosis (Rokitansky-Aschoff sinuses) in the gallbladder.

The significance of increased intraluminal pressure and intramural pathology in producing intramural diverticulosis in both cases is discussed.

Five roentgenograms.

CAPT. SAMUEL S. KRIKORIAN, M.C.
Lackland AFB, Texas

Impaction of Food Bolus in the Esophagus. Louis Pelner and Abraham H. Levy. *J.A.M.A.* 172: 1922-1923, April 23, 1960. (1352 Carroll St., Brooklyn 13, N. Y.)

A case of impaction of a food bolus in the esophagus is reported. The patient, a 76-year-old woman, complained of severe pressure in the retrosternal area for a week. An esophagram revealed a tangerine-sized area of radiolucency occupying the lower end of the esophagus at the fundo-esophageal junction. On close questioning, the patient recalled that all her symptoms started after she had swallowed a large mouthful of fish roe. Before subjecting this emaciated patient to esophagoscopy, it was decided to give enzymatic digestion a short trial. An enzyme powder containing 200 mg. of pepsin, 100 mg. of pancreatin, and 100 mg. of diastase per gram (Peptenzyme), 1/2 teaspoonful in 1/2 glass of water, was prescribed to be sipped slowly and repeated every two hours. After three doses of this preparation, roentgenograms revealed a definite alteration in the contour and outline of the mass, with beginning disintegration. Several days later this was complete and the mass had disappeared. A residual mild degree of achalasia was present.

Four roentgenograms.

RICHARD H. GREENSPAN, M.D.
New Haven, Conn.

Acquired Syphilis of the Stomach. Report of Two Cases. R. N. Cooley and J. H. Childers. *Gastroenterology* 39: 201-207, August 1960. (University of Texas Medical Branch, Galveston, Texas)

Syphilis of the stomach is uncommon, probably occurring in less than 0.1 per cent of persons with secondary or tertiary syphilis. The authors report 2 cases seen during an eight-month period. Bockus (*Gastroenterology*, W. B. Saunders Co., 1943, Vol. 1, pp. 712-741) lists five criteria for the diagnosis of gastric syphilis: (1) untreated tertiary syphilis, (2) a defect demonstrable roentgenographically, (3) presence of gastric symptoms, (4) inability to alleviate these symptoms or effect any improvement in the anatomical defect by orthodox management without antisymphilitic therapy, and (5) symptomatic relief with disappearance of the roentgen defect after intensive specific treatment. The authors recommend an additional criterion, namely, that tissue from the stomach removed for biopsy should show histologic changes compatible with syphilis.

The diagnosis should be suspected in a young patient with untreated syphilis who has a history of gastric symptoms longer than is usual for carcinoma. Weight loss is more gradual and massive hemorrhage less frequent than with carcinoma. Achlorhydria is common and is of some help in excluding peptic ulcer.

Differentiation of syphilis from carcinoma of the stomach is difficult, but certain roentgen features, when correlated with clinical and serologic tests, permit a considerable degree of diagnostic accuracy. Carman

(Roentgen Diagnosis of Disease of Alimentary Canal, Ed. 2, 1920) summarized the roentgen findings in gastric syphilis as follows: (1) a filling defect without a palpable mass, (2) hourglass stomach or a dilated body and fundus above with a concentric contraction of the antrum, (3) diminution in gastric capacity, (4) stiffening of the stomach wall with absence of peristalsis, and (5) infrequent pyloric obstruction. Both of the authors' cases appeared to fulfill the requirements for a diagnosis of gastric syphilis, yet each patient was believed pre-operatively to have a malignant tumor. In both cases the distal one-third to one-half of the stomach was involved, with some narrowing and irregularity. In the first there was an irregular hourglass deformity and achlorhydria. There were also multiple ulcers, but most of these were superficial and not visualized roentgenologically. In retrospect both lesions should have suggested the possibility of syphilis, but neither the radiologist nor the clinician adequately appreciated the significance of the strongly positive serologic test.

The greatest obligation of the radiologist is to suspect the presence of gastric syphilis and to alert the referring physician to this possibility. He also has a role in following the changes after specific treatment.

Six roentgenograms; 2 photomicrographs.

MAJ. MARTIN A. THOMAS, M.C.
Lackland AFB, Texas

Anastomosis Ulcers in Gastric Resection. E. de Arzuza Zulaica. *Rev. clín. españ.* 77: 393-403, June 30, 1960. (In Spanish) (Bilbao, Spain).

This title refers to ulcers at or within 5 to 10 cm. of the anastomosis between the gastric remnant after resection and the duodenum or jejunum. Estimates of their incidence vary from 5 to 21 per 100. These ulcers occur more commonly in men. They are more frequent following resection for duodenal ulcer and rare after benign gastric ulcer or gastric carcinoma (due to the higher gastric acidity associated with duodenal ulcers). The average time of occurrence is two to three years after surgery. Most are in blood group O patients.

Pain is essentially the same as that associated with ordinary ulcers, but may be more severe and vary more in location. It soon becomes continuous, without relief by alkalis.

The x-ray diagnosis is not always easy after Billroth II resection, because of superimposition of the jejunum and its folds. If the ulcer is on the suture line, its recognition becomes even more difficult. Dumping of barium obscures the changes in the jejunum, and compression, manipulation, etc., are difficult. It is necessary to examine at least 5 to 10 cm. of jejunum beyond the anastomosis, both afferent and efferent. This means that fairly large films should be used, so that the field will include enough small bowel. Examination in the erect position, with compression, separates the loops well. Films should be made with and without compression, and also in the supine position. One should begin with small amounts of barium and not fill the stomach too rapidly.

Folds near the niche may be thick, rough, or stellate, converging at the niche. Signs of jejunitis, rigid contours, thickened folds, etc., must be sought. Stenosis near the ulcer, narrowing of intestinal loops proximal or distal to the ulcer, or atonic dilatation are all indirect signs.

These lesions may be single or multiple. They are of variable size, up to 5 cm., and the large ones are some-

times missed. The appearance varies, depending on which projection they are seen in; and they may be round, oval, triangular, or stellate, with vague or sharp margins. Gastroscopy is difficult and often dangerous.

Medical management probably is not too valuable. If the earlier surgery was of the Billroth I type, a Billroth II and vagotomy should be performed. If the patient has already had a good Billroth II resection, a thoracic vagotomy should be done. Total gastrectomy is not recommended.

Statistics are presented in two tables.

Forty roentgenograms.

DON E. MATTHIASEN, M.D.
Phoenix, Ariz.

Roentgen Diagnosis of Certain Small Bowel Abnormalities. James G. Snead. *Virginia M. Monthly* 87: 429-435, August 1960. (603 Medical Arts Bldg., Roanoke, Va.)

The paper is of a general character, dealing with some of the more common small-bowel abnormalities. The conditions specifically discussed include chronic duodenal dilatation and stasis or "duodenal ileus," intra-abdominal and periduodenal hernias, and various tumors of the small bowel. Illustrative cases are summarized and suitable roentgenograms are reproduced. Those desiring background information on small-bowel diseases and their demonstration by simple radiographic methods will find this article helpful.

JAMES W. BARBER, M.D.
Cheyenne, Wyo.

Stilboestrol, Phenobarbitone, and Diet in Chronic Duodenal Ulcer. A Factorial Therapeutic Trial. S. C. Truelove. *Brit. M. J.* 2: 559-566, Aug. 20, 1960. (Radcliffe Infirmary, Oxford, England)

The results are presented of a therapeutic trial of three agents, namely, stilboestrol, phenobarbitone, and a gastric diet, on the course of duodenal ulcer in 80 men. Only patients with a typical history of duodenal ulcer of at least a year duration, in whom an actual ulcer crater could be identified radiographically were included. The trial was a carefully controlled one and was "double blind" so far as phenobarbitone and stilboestrol were concerned. All eight possible combinations of the three agents were used within the framework of a randomized block design. Patients on stilboestrol received 0.5 mg. twice daily and those on phenobarbitone 1 gr. twice daily. The actual trial period lasted six months, and the patients were then kept under observation for another five years.

Short-Term Results: At the end of the six-months trial period, all the patients were given a barium meal examination. At this time the radiologist was unable to identify an ulcer crater in 24 patients. One-half of those receiving stilboestrol showed radiological healing of the ulcer compared with only one-tenth of those not receiving this treatment, a difference which statistically is highly significant. Freedom from severe symptoms was almost universal among individuals on stilboestrol. Neither phenobarbitone nor a gastric diet had any material influence on either the short-term or long-term course of the disease.

Long-Term Results: An impressive feature of the results was the prognostic significance of the x-ray findings at the end of the six-months trial period. With a single exception, all 24 patients who no longer had a radiologically demonstrable ulcer crater at the end of

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the trial period remained symptom-free, with persistent radiological signs of healing, during the next five years. By contrast, most of the remaining patients had recurrent bouts of symptoms, and only a minority were symptom-free over a prolonged period and showed radiological healing at the end of the five-year follow-up. The beneficial effect of stilbestrol was chiefly evident in those patients with an ulcer history of less than an arbitrary period of ten years.

Complications of treatment were extremely mild, consisting of slight gynecomastia in a few instances and a hard to evaluate "decrease in full sexual potency" in some cases. When treatment ceased, the gynecomastia disappeared promptly and sexual potency returned within a week or two.

The author concludes that stilbestrol cannot be regarded as an ideal treatment for duodenal ulcer in men, because it is not universally beneficial and it produces side-effects. It should certainly not be employed in patients with a long history of ulcer. The possibility of obtaining the same benefits from a shorter period of stilbestrol treatment remains to be investigated.

The manner in which stilbestrol promotes ulcer healing is discussed.

Four roentgenograms; 2 graphs; 5 tables.

JAMES W. BARBER, M.D.
Cheyenne, Wyo.

Preoperative Diagnosis of Rupture into the Duodenum of an Aortic-Homograft Anastomosis. Report of a Case. I. Nik Nevin, Warner S. Bump, and George R. Thurer. *New England J. Med.* **263**: 243-245, Aug. 4, 1960. (St. Mary's Hospital, Rhinelander, Wisc.)

A late complication of aortic-homograft anastomosis is the formation of a "false aneurysm" immediately adjacent to the site of the anastomosis. This aneurysm can assume a large size and often gradually bores its way into the contiguous duodenum. Massive gastrointestinal bleeding is the inevitable result. It is important that an early correct diagnosis be made, if a prompt, life-saving operation is to be successfully carried out.

Salient points in making the diagnosis are: (1) a history of a previous operation for an aneurysm; (2) palpation of a pulsating abdominal mass; (3) an x-ray examination which reveals a density (soft-tissue mass) in close proximity to the vertebral column, with or without linear calcifications. Often, a single lateral view of the abdomen is sufficient to show an aneurysm if one is present. If the patient's condition permits, a barium meal can demonstrate a "filling defect" produced by the aneurysm in the duodenum. A case is reported in which a correct diagnosis of rupture of an aortic-homograft anastomosis into the duodenum was made on the basis of the above criteria.

Routine periodic roentgenography of the abdomen in lateral projection is recommended in all patients with surgically treated aortic aneurysms. It is believed that by this practice the formation of a new aneurysm can be detected and corrected before an emergency situation develops.

One roentgenogram.

D. I. COPE, M.D.
Mercy Hospital, Pittsburgh, Penna.

Uterine Leiomyoma as a Cause of Small Bowel Obstruction. A Case Report of Tumor Eroding the Intestine and Flaking Calcification into the Bowel Lumen. Earle E. Little and Howard J. Barnhard. *Am. J.*

Roentgenol. **84**: 281-284, August 1960. (University of Arkansas Medical Center, Little Rock, Ark.)

The authors present a unique case in which a calcified uterine leiomyoma eroded the terminal ileum and caused its partial obstruction. The patient was a 60-year-old Negro woman who complained of profuse vomiting for one week, intermittent episodes of cramping left lower quadrant abdominal pain, and a 50-pound weight loss during the previous two months. There had been no change in bowel habits and no melena. Gynecologic examination demonstrated an irregularly enlarged uterus with a large anterior mass thought to be a leiomyoma. Roentgenograms showed calcific flakes in the left abdomen, which were correctly considered to have come from the leiomyoma. A barium-enema study was of help in localizing the calcifications within the small bowel. A segmental resection of the involved bowel and a total hysterectomy were performed. No evidence of malignancy was found on histologic examination of the surgical specimen.

A search of the literature revealed many examples of leiomyoma which produced small and large bowel obstruction by extrinsic pressure, but no case in which a benign tumor had caused obstruction after erosion through the intestinal wall. One possible explanation of this occurrence, and that favored by the authors, is that adhesions united the leiomyoma with the bowel wall. As the myoma grew, the wall became stretched with compromise of its blood supply, necrosis occurred, and the tumor entered the bowel.

Three roentgenograms; 1 photograph.

ALFRED TENAGLIA, M.D.
St. Vincent's Hospital, New York

Concerning the Peutz Syndrome. H. Hartweg and R. Goerlich. *Fortschr. a. d. Geb. d. Röntgenstrahlen* **93**: 203-211, August 1960. (In German) (Medizinische Strahleninstitut, Tübingen, Germany)

The Peutz syndrome, also known as Peutz-Jeghers syndrome, is a rather rare familial condition, characterized by punctate melanotic pigmentation of skin and mucosa and by intestinal polyposis. The skin lesions are mostly facial, occurring especially around the lips, and on the dorsal aspect of hands and wrists. Here the spots are much darker and smaller than freckles; in the oral mucosa, they are not quite as small.

Intestinal polyps may occur anywhere from the nasopharynx downward to the rectum, but are found predominantly in the small bowel. They are the most important part of the syndrome, as they may cause colicky abdominal pain, intussusception, and anemia from occult bleeding.

Roentgenologically, the polyps may easily escape detection, as they can be rather small, far apart, and solitary. The roentgenologist, however, may be alerted by observing the pigmentation of face and hands, and by the clinical demonstration of anemia and occult bleeding. Thus, he can immediately direct his efforts toward finding intestinal polyps. The authors prefer to do a barium enema study first and an upper gastrointestinal series afterward.

Three cases are reported and well illustrated. The first patient was a woman, aged 23, with a history of bleeding nasal polyps. Like her father and two brothers, she had typical melanotic pigmentation of the skin and oral mucosa. Roentgenologic study revealed polyps in stomach and jejunum.

The second patient was the father of the first, aged 55. Like his daughter, his own father, and grandfather, he had characteristic pigmentation of the face. At one time, he almost had been operated on for so-called appendicitis because of transient colicky abdominal distress. Roentgen study revealed multiple polyps in the proximal parts of the jejunum. Since he had been free of symptoms for the preceding thirty months, there was no indication for an immediate surgical procedure.

The third patient was a girl, aged 19, with typical Peutz pigmentation and periodic abdominal pain since early childhood. Medication, including anthelmintics, proved ineffective. At the age of fifteen, the patient had been operated on for acute ileus, caused by a pedunculated small intestinal polyp. At seventeen years of age, she underwent a second laparotomy for intussusception of the small intestine. Again a large polyp was found. A week later, an additional intussusception necessitated an emergency operation with resection of the distal ileum and of a large polyp. Three weeks later, the splenic flexure of the colon was resected because of a large polypous growth in the descending colon.

This last case illustrates the tendency of frequent intussusceptions necessitating repeated emergency laparotomies. It also shows the importance of searching for multiple polyps as a cause of occult bleeding as early as possible and suggests the advisability of prophylactic small resections for the prevention of intussusception, infarction, and gangrene of intestinal segments.

In the differential diagnosis one must exclude familial-hereditary polyposis of the colon, which is potentially more malignant and is not as rare as the Peutz syndrome.

Eight roentgenograms; 2 photographs.

ERNEST KRAFT, M.D.
Northport, N. Y.

Diagnostic Accuracy of the Barium Enema Study in Carcinoma of the Colon and Rectum. R. N. Cooley, C. H. Agnew, and G. Rios. *Am. J. Roentgenol.* 84: 316-331, August 1960. (University of Texas—Medical Branch, Galveston, Texas)

The accuracy of the barium-enema examination in the diagnosis of 228 consecutive cases of carcinoma of the colon is assessed. A correct diagnosis was made by the barium enema in 103 instances, by proctoscopy and finger in 109, and by surgery and autopsy in 16. One hundred and seventy-nine of the 228 patients had one or more preoperative barium-enema examinations; during the period covered 12,250 barium-enema studies were performed, giving an incidence of carcinoma of 1.5 per cent.

The carcinoma was proximal to the rectum in 130 patients, and in 109 of these one or more preoperative barium-enema examinations were carried out. In this group, a tumor was overlooked 11 times, giving a false negative error of about 10 per cent; in 5 cases this resulted in a significant delay in treatment. Two errors occurred in a single patient who had three simultaneous tumors.

The authors employed a variety of technics, but in general the standard examination was performed, employing pre- and post-evacuation large films and a number of spot films. Various special views were taken at one time or another.

In 22 of 28 cases of carcinoma of the appendix and

cecum, a barium enema was used; the lesion was missed in 6, giving a false-negative error of 27 per cent. Two of the tumors were subsequently diagnosed by barium-enema study. Errors in the cecal area were due to failure to fill the cecum, failure to obtain adequate mucosal detail (associated, in most instances, with imperfect emptying of the cecum), failure to appreciate the varied manifestations of carcinoma in this area, or simple human failure to recognize an obvious lesion.

Thirty-six cases of primary tumor of the segment between the cecum and sigmoid colon were encountered, and a barium-enema examination was performed in 35 of these. In all but 1 the lesion was correctly diagnosed, the single exception being a carcinoma of the left transverse colon.

Fifty-two of 66 patients with carcinoma of the sigmoid colon had at least one barium-enema study; the lesion was correctly diagnosed in 48 of these, giving a false-negative error of about 8 per cent. In the sigmoid, the differentiation of diverticulitis or diverticulosis from neoplasm was a recurring roentgenologic problem.

Carcinoma of the rectum is difficult to diagnose roentgenologically, and in 34 of 70 patients with a tumor in this area, the lesion was not visualized on barium-enema examination, a false-negative error of 49 per cent. The radiologist was aware of the diagnosis in the majority of cases but seemed to make no determined effort to demonstrate the lesion.

In the present series the causes of error were varied but were predominantly poor technic, inexperience, and momentary individual lapses. Some of the errors, the authors believe, were unavoidable. Recommendations for improved performance are given.

Twenty-three roentgenograms; 1 diagram; 7 tables.

PAUL MASSIK, M.D.
Quincy, Mass.

Cathartic Colon. Richard H. Marshak and Arnold Gerson. *Am. J. Digest. Dis.* 5: 724-727, August 1960. (1075 Park Ave., New York 28, N. Y.)

The authors report a case of "cathartic colon" to re-emphasize the roentgen features which help to distinguish this entity from so-called "burnt out" ulcerative colitis (see also, Heilbrun: *Radiology* 41: 486, 1943, and 65: 549, 1955). Roentgenologically, the most severe changes are seen in the proximal colon and consist of absent or diminished haustral markings, bizarre contractions, and inconstant areas of narrowing. The bowel is moderately distensible in contrast to the rigid tubular bowel of "burnt out" ulcerative colitis. Barium is frequently retained in the colon after evacuation. The mucosal pattern shows no evidence of ulceration. In the more severe cases, the left side of the colon is also involved, but the sigmoid and rectum remain distensible. The terminal ileum may show changes similar to those in the right side of the colon for varying lengths. The ileocecal valve is frequently flattened and gaping. Fluoroscopically and on roentgenograms, tubular areas of narrowing are demonstrable; these narrowed areas are inconstant and may disappear during a single examination or vary in extent. The patient's history is characteristic: the ingestion for many years of drastic irritant cathartics that have their action primarily on the colon.

Six roentgenograms.

WILLIAM H. ELLSWOOD, M.D.
Charleston, West Va.

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Megacolon: Evaluation of a Method for Experimental Production of Aganglionosis. Philip M. Johnson, Margaret C. Swanton, Charles A. Bream, and Richard L. Murtland. *Ann. Surg.* 152: 313-319, August 1960. (P. M. J., 98 Warren Place, Montclair, N. J.)

An investigation was undertaken to evaluate the experimental observation that dilute phenol is a selective ganglionic agent when injected into tissues containing ganglion cells. Ten cats were used in the experiment, with 1 serving as a control. The abdominal cavity of each experimental animal was opened, and 1 to 2 milliliters of a 5 per cent phenol solution was injected between the muscle coats of the colon around the entire circumference, producing an edematous ring-like strip at least 1 cm. in width. The control underwent the same surgical procedure, with the injection of 2.0 ml. of sterile water instead of phenol. Six animals were examined by barium enema on the seventh or eighth postoperative day. At this time, the colon of the control cat was normal. The other 5 animals exhibited changes at the injection site which ranged from slight smooth constriction to marked irregular stenosis with evidence of intramural fistulas and extravasation of barium into the peritoneal cavity. Four animals were examined twenty-eight to thirty-five days postoperatively. Three had a smooth ring-like stenosis at the injection site. One animal which had had localized perforation of the colon on the eighth operative day displayed no abnormality of the colon at four weeks. In another, which had had marked irregular narrowing of the lumen on the eighth day, the colon was normal on the twenty-eighth day.

Since the interstitial injection of dilute phenol resulted in destruction not only of ganglion cells but also of all tissues with which it came in contact, the material is unsuitable for selective aganglionosis production in the laboratory animal.

Five roentgenograms; 4 photomicrographs; 2 photographs; 1 table.
ZAC F. ENDRESS, M.D.
Bloomfield Hills, Mich.

Profile Lateral Projection in the Diagnosis of Lesions of the Rectum. Henry C. Forrester and A. Bradley Soule. *Am. J. Roentgenol.* 84: 332-338, August 1960. (The Mary Fletcher Hospital, Burlington, Vt.)

This is a brief article on an old subject, pointing out the value of a lateral projection of the lower colon to supplement other views. This method has been routinely employed for the past eleven years in the area in which the authors practice and has helped in the demonstration of cancers, polyps, adhesions, and other lesions. They described it earlier in *Acta radiol.* 53: 113, 1960. (*Abst. in Radiology* 76: 508, 1961). This projection does not take the place of air contrast in a search for polyps.

Twenty-three roentgenograms.

PAUL MASSIK, M.D.
Quincy, Mass.

Contribution of Cineradiography to Study of the Function of the Human Biliary Tract. J. Caroli, P. Porcher, G. Pequignot, and M. Delattre, with the technical collaboration of M. Becker and R. Hougrand. *Am. J. Digest. Dis.* 5: 677-696, August 1960. (Saint Antoine Hospital, Paris, France)

The authors employed cineradiography and manometry to study the biliary tree in 34 patients, with partic-

ular emphasis on the function of the sphincter of Oddi. Their technic entailed the use of an indwelling catheter in the biliary system. The contrast agent was Diodone 35 per cent. The radiographic equipment, projection equipment, and the ancillary devices used for this study are described in detail.

It was found that the type of contraction of the sphincter of Oddi may vary in the same subject. The amplitude of the contraction differs greatly from one individual to another.

The kinetics of contraction and relaxation were studied with a timer. As shown in one of the authors' cases, the duration of the opening and closing phase was the same when perfusion conditions were the same. With residual pressure (12-18 cm. water), the absolute duration of each phase was three seconds. Elevation of the perfusion pressures from 18 to 35 cm. water, instead of accelerating the basal rhythm, slowed it. The effects of relaxing agents (atropine, amyl nitrite, fatty meals) and contracting agents (morphine, chlorpromazine) were also investigated. Relaxing agents increased the duration of the opening phase of the sphincter and decreased the closure phase, whereas morphine had an opposite and more drastic action on the sphincter.

The cineradiomanometric studies disclosed an incidence of pancreatic reflux of 30 per cent. It is mentioned that pressures high enough to result in pain were not used and that several of the examinations were not carried out under general anesthesia, by which means the best refluxes could be obtained; these limitations could account for the somewhat low incidence of reflux.

When common duct pressure was increased and relaxation of the sphincter of Oddi obtained, reflux into the duct of Wirsung was favored, provided anatomic conditions were normal. This phenomenon did not hold true under abnormal conditions.

Twenty-three roentgenograms.

WILLIAM H. ELLSWOOD, M.D.
Charleston, West Va.

Cholecystography with Bunamiodyl. William T. Meszaros and Frederick M. Rich. *J.A.M.A.* 172: 1884-1887, April 23, 1960. (1853 W. Harrison St., Chicago 12, Ill.)

Bunamiodyl (Orabilex) was employed in a standard six-capsule dose (4.5 gm.) in 500 patients referred for routine cholecystography. The incidence of side-effects such as nausea (14 per cent), vomiting, diarrhea, cramps (4 per cent each), and dysuria (2 per cent) was significantly lower than has been reported for other commonly used contrast agents. Fair, good, or excellent visualization of the gallbladder was obtained in 364 examinations (72.8 per cent), and poor visualization in 34 (6.8 per cent). The gallbladder was not visualized in 102 patients (20.4 per cent). Fifty patients were given a fat meal; the cystic duct was visualized in all and the common duct in 19 (40 per cent). Residual contrast medium seen in the colon was minimal to none in 368 cases (73.6 per cent), moderate in 116 (23.2 per cent), and dense in 16 (3.2 per cent); in no instance did it interfere with diagnosis.

There was no follow-up of patients with non-visualized gallbladders, and no correlation of the pathologic and the cholecystographic findings is presented.

Three roentgenograms; 4 tables.

RICHARD H. GREENSPAN, M.D.
New Haven, Conn.

Opacifying Gallstones. Utility of a New Examination for the Demonstration of Duct Stones Useful in the Presence of Jaundice. David H. Watkins and Emanuel Salzman. *Arch. Surg.* 80: 986-991, June 1960. (650 Madison Ave., Denver, Colo.)

Opacification of radiolucent biliary calculi may occur after repeated doses of Telepaque (iopanoic acid) (Salzman and Warden: *Radiology* 71: 85, 1958). This procedure has been called "biliary calculography," and the stones having this quality, "opacifying gallstones." There is usually a generalized faint increase in the shadow of the stone, with a sharp linear density outlining the periphery. This opacification phenomenon is probably due to the deposition of the contrast material on the surface of the stones. After a four-day iopanoic acid test the opacification of the stones persists for a variable period of time, ranging from two to fourteen days.

In a series of 120 patients examined with the four-day iopanoic acid test, there were 13 proved cases of bile duct stones. In 10 of these opacifying stones in the ducts were demonstrated.

Although a larger experience is needed for definitive conclusions, it is apparent that the four-day iopanoic acid test is a useful method for identifying bile-duct stones. These have been visualized in patients with intact gallbladders and also in the postcholecystectomy state. The test has also been useful in positively demonstrating duct stones suspected on "T-tube" cholangiography. Biliary calculography is probably the most useful procedure for demonstrating bile duct calculi in the presence of jaundice and for showing calculi within the intrahepatic ducts. All methods fail to visualize the ducts or identify bile-duct calculi in the patient with a high degree of duct obstruction or liver insufficiency.

Ten roentgenograms.

The "Four-Day Telepaque Test" in the Investigation of the Post-Cholecystectomy Syndrome. Glyn A. S. Lloyd. *Brit. J. Radiol.* 33: 522-523, August 1960. (St. Mary Abbots Hospital, Kensington, W. 8, England)

The author reports a case to illustrate the usefulness of the four-day Telepaque test in the investigation of the post-cholecystectomy syndrome. In this case the four-day test disclosed calculi in the common duct which had not been visualized on intravenous cholangiography. The bile ducts were also outlined more clearly than by the intravenous method. The four-day Telepaque test is most likely to be successful in patients with elevated serum bilirubin and slight to moderate jaundice, and it is in precisely these cases that intravenous cholangiography is often inadequate.

Three roentgenograms.

CAPT. SAMUEL S. KRIKORIAN, M.C.
Lackland AFB, Texas

Intravenous Cholangiography in Biliary Tract Disease. George Johnson, Jr., Charles Pearce, and Frank Glenn. *Ann. Surg.* 152: 91-102, July 1960. (New York Hospital-Cornell Medical Center, New York, N. Y.)

Data on 213 patients upon whom intravenous cholangiography was attempted prior to surgery on the biliary tract are presented. During the six-year period (1953-58) in which these patients were studied, more than 2,500 intravenous cholangiographic examinations were performed without a serious reaction. A standard technic was employed, with delayed films and tomograms added as indicated.

Visualization of the common bile duct sufficient for interpretation was obtained in 128 (60.1 per cent) of the 213 patients. In 54 of the 85 patients with non-visualization, the serum bilirubin was elevated. A previous report from the New York Hospital-Cornell Medical Center emphasizes that elevation of the serum bilirubin is associated with a decreased likelihood of demonstrating the biliary tree, with consistent failure when the amount rises above 3.0 mg. per cent. No correlation between elevation of serum alkaline phosphatase and visualization of the biliary ductal system could be established.

The common duct was visualized in 76 (65.5 per cent) of 116 patients in whom no abnormalities of the duct were evident at operation. In only one instance was choledocholithiasis reported and in only 3 cases was dilatation thought to be present radiographically. The serum bilirubin was slightly to markedly elevated in 14 of the cases with non-visualization, and normal or undetermined in the remaining 26.

The common duct was demonstrated in 41 (62.1 per cent) of 66 patients in whom common duct calculi were found at surgery; cholangiograms had revealed calculi in 24 of the 41. Dilatation without stones was reported in an additional 7. Failure to visualize the common duct in the patients with choledocholithiasis was associated with elevation of the serum bilirubin in 22 of 25 patients, in 12 to 3.0 mg. per cent or higher.

Visualization of the common bile duct was obtained in half of 22 patients in whom dilatation of the common bile duct without calculi was shown. Calculi were subsequently found in 2 of these. Hyperbilirubinemia was present in 9 of 11 cases in which the duct was not demonstrated.

Intravenous cholangiography failed to show the common duct in 6 cases of stricture of that structure. The serum bilirubin was elevated in all of these cases.

Although the gallbladder was visualized in only 39 of 109 cases of chronic cholecystitis, oral cholecystography had also failed to reveal the gallbladder in many of the patients, and in some, detailed films at two hours or longer after injection were not made. When the cholecystogram was evident, however, calculi were demonstrated with a high degree of accuracy.

In not one of 39 cases of acute cholecystitis was the gallbladder visualized. The common bile duct was demonstrated in 22 cases.

A cystic duct remnant was visible on intravenous cholangiography in 4 patients; 3 of these contained calculi which were correctly identified on the cholangiogram. In 14 additional patients a cystic duct remnant was excised; in most of these cases calculous disease of the common bile duct was evident on intravenous cholangiography, although the cystic duct remnant had not been visualized.

The authors conclude that intravenous cholangiography is particularly useful in the evaluation of the common bile duct and its tributaries. Following cholecystectomy, persistence or recurrence of upper abdominal symptoms sometimes occurs. In the patient suspected of choledocholithiasis but not frankly jaundiced, the demonstration of calculi within the common duct by intravenous cholangiography may often establish the diagnosis.

Thirteen cases are reported.

Seven roentgenograms accompanied by drawings; 7 tables.

RICHARD H. GREENSPAN, M.D.
New Haven, Conn.

HERNIA

The Diagnosis of Epiphrenic Ampulla. E. de Arzúa Zulaica. *Rev. clín. españ.* 78: 212-219, Aug. 31, 1960. (In Spanish) (Bilbao, Spain)

The diagnostic signs of hiatus hernia and epiphrenic ampulla are outlined by the author, following his experience with 250 hiatus hernias in 4,470 patients. All examinations were carried out with fluoroscopy and radiography during barium swallow in semi-prone, mild Trendelenburg position.

Special attention is necessary during the first swallow, since this often is diagnostic. In hiatus hernia there is an interruption in the esophageal barium column, and the hernia then fills, showing a larger diameter than the esophagus proper, with more or less irregular borders. Ampullas form and are seen on later swallows, when the patient by inspiration closes the esophageal hiatus. There is no interruption of the barium column in the first moment. The interruption, when it does develop, occurs later. At times the separation is not seen in hiatus hernia, as if the esophagus and hernia were continuous, and the walls may be more elastic with regular contour.

In typical cases the hernias are irregular, and the right border of the esophagus in its lower third shows accordion-like folds. Diameters may be from 3 to 4 times that of the esophagus with nonuniform density and variable tonicity. The collar is wide, and folds are gastric, thick, irregular, and more numerous than in the esophagus. On emptying, the barium-covered folds, whether or not outlined with air, keep the same appearance, and the serial demonstration of differences in tonicity is characteristic. Changeability of size and shape is seen on serial films, and emptying is slow and passive.

Unlike hiatus hernias, epiphrenic ampullas have regular contour, are symmetrically round or oval, have the same tone as the esophagus, are elastic, and are never more than two or three times the caliber of the esophagus. The folds are fine and regular, they are continuous with the esophagus, and they change volume, but less so than hiatus hernias. They empty rapidly with the first expiration, after having filled on inspiration. They all show the same tonicity.

One has to keep in mind that there may be atypical cases. The signs enumerated show little variation and confusion with hiatus hernias is unusual. Hiatus hernia, however, can be misdiagnosed as ampulla. Moreover, the two can be associated. When a hiatus hernia is behind the esophagus and its upper limit is confused with the lower end of the esophagus, it may simulate an ampulla. To differentiate them, fluoroscopy is essential to show that the ampullas form with inspiration and empty with expiration, while the hernia remains the same in both phases. (Radiographs in the two phases of respiration are not always dependable, due to technical variations, timing of swallows, etc.) Sometimes the ampulla has double borders with a thick central fold, but its margins are always parallel, which never occurs in superimposition of ampulla and hernia.

When the superior margin of a hernia fades gradually into and is continuous with the esophagus, its collar may be broader than its body. This is never seen with an ampulla.

Sometimes, to determine whether gastric folds are above or below the diaphragm, one must obtain films in inspiration and expiration, remembering that the

hiatal portion of the diaphragm is higher than the rest in inspiration and lower in expiration.

Twenty-one roentgenograms.

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THE SPLEEN

Roentgen Findings in Splenic Hemorrhage. John R. Amberg, Julio P. O'Laco, and William A. Wilcox. *Wisconsin M. J.* 59: 363-365, June 1960. (Milwaukee County Hospital, Milwaukee, Wisc.)

Twenty-five cases of ruptured spleen, with surgical or autopsy proof of splenic hemorrhage, were reviewed. In only 10 of these cases were roentgenograms of the abdomen obtained; the findings were abnormal in 9. Review of the films disclosed no single roentgen pattern but a family of patterns, reflecting in general the extent of the intraperitoneal hemorrhage.

The sequence of events following splenic rupture can be divided into four stages, with the corresponding roentgen findings, as follows:

Stage I: Intrasplenic bleeding. Rupture of capsule. Slight enlargement of splenic shadow (most often difficult or impossible to identify).

Stage II: Perisplenic hematomas. "Tamponade" by adjacent viscera. Distinct increase in size of the "splenic" shadow. Gastrectasia and ileus. Alterations in the contour of the stomach and the splenic flexure of the colon.

Stage III: Bleeding, extending down left gutter. Diffuse haziness in left flank region. Descending colon may be displaced medially. Straightening of the peritoneal fat line on the left.

Stage IV: Bleeding, with diffuse intraperitoneal spread. Separation of loops of small bowel, diffuse clouding of the abdomen, and bulging of flanks.

All four stages may occur in a matter of minutes following severe splenic trauma or the hemorrhage may temporarily cease at any stage. Diagnosis is most difficult when hemorrhage from the spleen is slow or delayed (up to a year or more after trauma) or when there is no clear history of trauma. Auxiliary roentgen findings in the present series were elevation of the left hemidiaphragm and left lower rib fractures in a few cases.

Three roentgenograms.

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THE MUSCULOSKELETAL SYSTEM

Eosinophilic Granuloma of Bone. A Study of Twenty-eight Cases. Malcolm H. McGavran and Herbert A. Spady. *J. Bone & Joint Surg.* 42-A: 979-992, September 1960. (Washington University School of Medicine, St. Louis 10, Mo.)

The authors present 28 previously unreported cases of eosinophilic granuloma of bone with emphasis on the distribution, differential diagnosis, and roentgenographic appearance of these lesions, with particular reference to their course as determined by long-term follow-up. The skull, femur, ribs, and mandible were the most frequent sites of involvement.

The roentgenographic appearances and diagnoses may justifiably be divided into two groups. Eosinophilic granulomas involving the *flat bones*, usually of the cranial vault, are sharply defined punched-out defects. Dermoid cyst and eosinophilic granuloma are the diag-

noses usually considered. In 7 cases with skull involvement, the authors did not see the button sequestra described by Wells (Radiology 67: 746, 1956). Only in later adult life might myeloma be considered, since a well documented case of this disease in childhood is almost unheard of. The lesions of the ilium and mandible are similar to those of the skull.

In the long bones no preference for a diaphyseal or metaphyseal location was found. The authors did not see eosinophilic granuloma involving the epiphysis. In children both diaphyseal and metaphyseal lesions are destructive processes with erosion of the cortex and moderate to marked periosteal new-bone formation. This last change, the onion-peel appearance, has on occasion been thought to be characteristic of Ewing's sarcoma. Expansion of the involved bone, when present, occurred by periosteal layering. The bone defects frequently appeared lobulated, with splotchy opacity representing irregular bone destruction rather than intrinsic calcification or ossification.

In adults the lesions of the long bones are chiefly diaphyseal and quite different from those in children. Eosinophilic granulomas in the long bones of adults are seen as indistinct, centrally placed radiolucencies with very little cortical erosion or periosteal reaction. The rib lesions are lobulated, destructive, and expansile, with slight periosteal reaction.

As with many bone lesions the roentgenograms give an excellent gross anatomical picture of the process, but unfortunately they are not diagnostic. The authors have seen cases of Ewing's sarcoma and osteomyelitis involving the long bones in children in which the roentgen findings were indistinguishable from eosinophilic granuloma. Thus, biopsy is imperative for diagnosis.

All 28 of the patients in the present series have done well on long-term follow-up and their lesions have healed regardless of the type of treatment employed.

The authors emphasize that the etiology of eosinophilic granuloma remains unknown. The transformation to Hand-Schüller-Christian disease or to Abt-Letterer-Siwe disease must be, if it does occur, very uncommon. The authors did not observe this transition in their 28 cases, and they have some doubts whether the recorded examples represent true changes from one form to another.

Sixteen roentgenograms; 1 graph; 2 tables.

MAJ. MARTIN A. THOMAS, M.C.
Lackland AFB, Texas

Degenerative Disk Disease of Cervical Spine. Clinical and Roentgenographic Study. Zachary B. Frieden-berg, Harold A. Broder, Jacob E. Edeiken, and H. Newton Spencer. J.A.M.A. 174: 375-380, Sept. 24, 1960. (Hospital of the University of Pennsylvania, Philadelphia 4, Penna.)

One hundred patients with an established diagnosis of degenerative disk disease of the cervical spine were examined to determine their clinical course and to find out if there was any correlation between the clinical and roentgenographic findings. A previous study by the authors demonstrated a close correlation between the roentgenographic and anatomic findings (J. Bone & Joint Surg. 41-A: 61, 1959. Abst. in Radiology 73: 816, 1959).

The sex distribution in the present series was equal, and symptoms most often began in the fifth decade. A definite traumatic incident was associated with the onset of symptoms in 25 patients. Nineteen patients

suffered only one attack of pain; 34 had intermittent attacks with varying symptom-free intervals, and in 47 pain was continuous. Eighty-three patients complained of pain in both the neck and arm, while 12 had symptoms mostly limited to the arm. Loss of strength in the upper extremities was noted by 35 patients.

Restriction of motion in the cervical spine was the most frequent finding (in 44 patients). Tenderness over the lower cervical spine was present in 23. Diminution or absence of the biceps and/or triceps reflexes occurred in 14. Patterns of sensory impairment varied widely, with the sixth and seventh roots most commonly affected.

The roentgenograms of each patient were classified as normal or Grade 1, 2, or 3, according to the progression of the following changes: disk narrowing, sclerosis of the adjoining body surfaces, osteophyte formation, and degenerative changes in the apophysial and lateral "joints" of Luschka.

The dermatomic distribution of pain radiating into the upper extremity and sensory impairment corresponded to those cervical levels of disk degeneration and reactive bone formation seen on the roentgenogram. There was, however, no correlation between the intensity of pain and the degree of roentgenographically visible change at the involved cervical disk level. Progression of neurologic findings was uncommon. No specific roentgen finding was associated with the development of symptoms. Disk degeneration with symptoms may be present in early stages without roentgenographically visible changes. In the more advanced stages, roentgen changes are invariably observed.

Patients responded well to different forms of therapy, but pain usually recurred.

Three roentgenograms; 5 graphs; 1 table.

WILLIAM MARTEL, M.D.
University of Michigan

Unilateral Laminar Joints of Lumbar Spine. Case Report. Malcolm D. Jones. J. Bone & Joint Surg. 42-A: 1076-1078, September 1960. (University of California Medical Center, San Francisco 22, Calif.)

According to Willis (Man's Back, 1953), 5 to 7 per cent of lumbar vertebrae have defects in the lamina which are usually fibrous zones in the bony arch. The occurrence of anomalous true joints in the laminae seems never to have been recorded. The author describes two anomalous true joints in one of the laminae of the third lumbar vertebra encountered in a spine in a collection in the Department of Radiology of the Montreal Neurological Institute. Initial roentgenograms of the specimen revealed an atypical spondylolysis of the third lumbar vertebra, located in the left lamina between the base of the spinous process and the pedicle. After section of the pedicles and removal of the vertebral bodies, roentgenograms were made of the posterior elements in the standard oblique projection. These showed two separate joints located side by side in the midportion of the left lamina. The articular surfaces of these joints were outlined by typical subchondral bone. When the soft tissues had been dissected away, each joint was found to have a separate capsule attached firmly to the lamina at the margins of the articular surfaces. The joints were separated by a complete defect through which a fine probe could be passed.

Two roentgenograms; 2 photographs; 1 photomicrograph.

MAJ. MARTIN A. THOMAS, M.C.
Lackland AFB, Texas

Instability of the Pubic Symphysis and Congenital Dislocation of the Hip in Newborns. The Possible Etiologic Role of Maternal Hormones. Lars Andrén. *Acta radiol.* 54: 123-128, August 1960. (Malmö Allmänna Sjukhus, Malmö, Sweden)

The concept that dysplasia of the joint is the primary cause of dislocation of the hip in the newborn was first challenged by Howorth (*Ann. Surg.* 125: 216, 1947), who suggested that congenital dislocation of the hip may be secondary to a gradual relaxation of the joint capsule or to a deformity of the acetabulum. On roentgen examination of a series of newborn infants with congenital dislocation of the hip, the present author noticed coexistent instability of the symphysis pubis. When the femoral head was pressed against the acetabulum and then dislocated posterolaterally, the manipulation was accompanied by a widening of the symphysis. A distinct relaxation of the capsule occurred, which stretched as the femoral head slipped out of the acetabulum.

Observations are recorded on 3 newborn girls with congenital dislocation of the hip who had a coexistent instability of the symphysis pubis. When they were examined on the first day of life, the symphysis pubis was found to widen from 4 to 7 mm., from 6 to 9 mm., and from 3 to 6 mm. in association with the examination. The difference in the distance between the femoral heads in the two positions was 10, 13, and 9 mm., respectively. In 38 of 40 normal newborn infants, the widening of the symphysis was less than 1 mm.; only in 2 was it as much as 1.5 mm. The greatest difference in the distance between the femoral heads in this group was 7 mm. (average 4 mm.).

It is suggested that the primary factor in the etiology of congenital dislocation of the hip is a marked reaction of the newborn to the maternal hormones resulting *inter alia* in a relaxation of the capsule of the hip joint and symphyseal instability. It is this relaxation of the capsule that makes partial or complete dislocation of the hip possible if the legs are held in an unnatural position during the first week or so of life. The inherited characteristic is the increased reaction to the maternal hormones and not the dislocation as such. Dysplasia is a secondary phenomenon.

Eight roentgenograms.

PETER TORBEY, M.D.
University of Washington

Roentgenographic Studies on Epiphyseal Growth and Ossification in the Knee. Sven Scheller. *Acta radiol. Suppl.* 195, 1960. (University of Gothenburg, Sweden)

This 300-page monograph reports an exhaustive study of the knees of 876 children (473 boys and 403 girls) from one to fifteen years of age. Evaluated were (a) dimensional growth, (b) morphogenesis, and (c) ossification pattern. In the proximal tibial epiphysis dimensional growth was assessed on the basis of an "epiphyseal index." The distal femoral epiphysis was evaluated as to "epiphyseal index" plus "condylar width," "condylar height," "medial condyle," and "lateral condyle." The conclusions reached are summarized in a 7-page statement which defies further reduction.

A short section on osteochondritis dissecans indicates the author's belief that in the knee it is due to a transchondral fracture secondary to trauma. He does not believe there is a relationship between osteochondritis dissecans and accessory ossification centers in the knee.

This monograph is recommended reading for anyone

having to deal with the vagaries of growth and development of the knee. It is abundantly illustrated by line drawings and roentgenograms.

HOWARD J. BARNHARD, M.D.
University of Arkansas Medical Center

Fractures at the Tuberosity of the Fifth Metatarsal Bone in Children. Herbert Müssbichler. *Acta radiol.* 54: 90-96, August 1960. (Karolinska Sjukhuset, Stockholm, Sweden)

Sixty-six fractures at the tuberosity of the fifth metatarsal bone (occurring in a total of 1,668 injuries to the feet and ankles in children) were studied with regard to frequency, type, and healing. The fractures were distributed equally among boys and girls, all but 1 of whom were over ten and a half years of age.

The lateral part of the base of the fifth metatarsal is formed by the tuberosity, which is usually part of the diaphysis. The growth of the tuberosity on its lateral and plantar aspects takes place in the epiphysis and there is considerable variation in size, shape, and position. The epiphysis is invariably present at the age of fifteen years.

The fractures in the present series were classified into the following types: (1) transverse fractures, 53 cases; (2) oblique and longitudinal fractures, which are regarded as atypical, 5 cases; (3) avulsions, 8 cases; (4) epiphyseal separation, 1 case.

The transverse fractures and the avulsions were all characterized by a prolonged healing time. The delayed union of the transverse type of fracture, as well as of the avulsions, is in all likelihood due to the effect of traction of the peroneus brevis muscle, which is inserted at the tuberosity. This results in an increase of the diastasis between the fragments. In children this will ultimately not interfere with healing, and complete union can be expected ten weeks or later after the injury. This series of events does not seem to be influenced to any apparent degree by the type of fixation applied. Eventually, in the author's cases, a complete union of the fragments always took place, irrespective of the treatment.

Twenty roentgenograms; 2 drawings.

PETER TORBEY, M.D.
University of Washington

THE GENITOURINARY SYSTEM

Sponge Kidney: A Review of the Literature and a Report of Five Cases. Benjamin S. Abeshouse and George A. Abeshouse. *J. Urol.* 84: 252-267, August 1960. (100 W. Monument St., Baltimore, 1, Md.)

The authors report 5 cases of "sponge" kidney. A search of the literature revealed 131 cases, only 12 of which came from the United States. [Since publication of this paper, the number has more than doubled. See Palubinskas: *Radiology* 76: 911, 1961, and Secrest and Kendig: *Radiology* 76: 920, 1961.—Ed.] The incidence of the condition is probably much higher than the above figures would indicate, as undoubtedly many cases go unrecognized. The most striking pathologic feature is the presence of multiple small cystic cavities in all the pyramids of one or both kidneys, which impart a porous or spongy appearance. If no complications supervene, the kidneys are of normal size and shape, with no appreciable alteration in function.

The condition was bilateral in 109 cases and unilateral in 27. Although the cystic process is diffuse, involving

all the pyramids of the affected kidney, the degree of involvement of each pyramid may vary. Only in the exceptional case are the changes limited to one pyramid of one kidney. The cysts are confined strictly to the pyramidal portion of the medullary zone, the cortical zone being devoid of lesions. Two types of cysts have been described: (1) an irregular type lined by cylindrical epithelium and consisting of large cells of an embryonic nature and (2) spheroidal cysts lined by flattened or thin epithelium. Calculi were found in the cystic cavities in 88 cases. When an acute or chronic infection is superimposed, inflammation and suppurative changes may be manifested within the cystic cavities.

Sponge kidney is predominantly a disease of males. In the cases reviewed the proportion was 92 males to 36 females (2.5:1). Sex was not ascertained in 8 cases. The disease was most frequently encountered in the fourth (21 cases), fifth (31 cases), and sixth (17 cases) decades.

Several theories have been offered in explanation of the development of sponge kidney, the most acceptable one being faulty ontogenetic development, *i.e.*, ectasia or dysplasia.

The sponge kidney produces no symptoms unless it is accompanied by infection, stone formation, or obstruction. Among the cases reviewed, hematuria was the most frequent complaint (65 cases); pyuria occurred in 57 cases, albuminuria in 22, fever in 13, and pain in 50.

The diagnosis is customarily made by excretory urography or retrograde pyelography, which will reveal the characteristic grape-like clusters of cysts filled with opaque medium and occupying each pyramid of the affected kidney. A plain roentgenogram is negative unless calculi are present within the cysts. In the differential diagnosis, various conditions must be considered, including the microcystic form of polycystic disease of the kidney; calyceal diverticula; cystic changes in the epithelial lining of the upper urinary tract; cysts of pyramids associated with acute or chronic pyelonephritis; pyelogenic cysts of the medulla; cystic cavities associated with renal tuberculosis; cystic cavities associated with renal calculi; nephrocalcinosis; cystic cavities associated with necrotizing or sclerosing papillitis; and changes in pyramids and pericalyceal tissues due to reflux of pyelographic medium.

There is no specific treatment for the uncomplicated case of sponge kidney; in the symptomatic case, therapy must be directed to the complications. The prognosis in the absence of calcifications is uniformly good (as opposed to that in polycystic kidneys); in complicated cases it must be guarded.

Nine roentgenograms; 1 photograph.

MARK M. MISHKIN, M.D.
University of Pennsylvania

Congenital Ureteral Valve in Children: A Case Report. Edward Passaro, Jr., and J. P. Smith. *J. Urol.* 84: 290-292, August 1960. (Ohio State University College of Medicine, Columbus 10, Ohio)

An authentic case of ureteral valve in a five-year-old girl is reported. For two years the patient had had attacks of sore throat, malaise, urinary incontinence, and fever to 102-104° F. She was incontinent night and day, and a foul odor was ascribed to the urine. There was frequency but no dysuria or hematuria during the attacks. Flank or abdominal pain had never been experienced.

The patient was well developed and well nourished

but appeared chronically ill. A blood pressure of 110/60 was recorded on several occasions. The specific gravity of the urine was 1.036, with 1 to 3 white blood cells per high-power field. The blood urea nitrogen was 10 mg per cent.

Intravenous pyelography showed a moderately hydronephrotic left kidney with a high ureteral block. Cystoscopy and retrograde pyelography revealed the presence of a contrast medium-displacing valve-like lesion approximately 2 cm. below the left ureteropelvic junction. No point of constriction, tenting, or convolution of the ureter was demonstrated.

On exploration, the normal ureteral peristalsis was seen to be interrupted 2 cm. below the ureteropelvic junction. Here the ureter was constricted and the proximal ureter was dilated. A firm transverse valve could be palpated at this point. On incising the ureter, an "iridic" valve with a small central opening was disclosed. A V-Y plasty was carried out, cutting through the valve wall. The ureter was reconstructed over a Cumming's catheter and brought out through a pyelostomy incision.

A congenital ureteral valve should be suspected when (1) a valve-like ureteral lesion containing smooth muscle fibers is encountered; (2) there is no obstruction proximal to this point; and (3) no other ureteral obstructive lesion is present.

Three roentgenograms; 2 photographs; 1 table.

JOSEPH M. WINSTON, M.D.
University of Pennsylvania

Post-Voiding Films as an Aid to Opacifying the Obstructed Ureter. Donald R. Rooney. *J. Urol.* 84: 300-306, August 1960. (Emory University School of Medicine, Atlanta, Ga.)

Urologists and radiologists are frequently confronted with the problem of unilateral nonvisualization on an excretory urogram. The author describes a simple technic for demonstrating the obstructed ureter. If, on routine excretory urography, there is an early nephrogram or any opacification of the calyces on the involved side, the patient is instructed to walk, when possible, to the rest room and to urinate. After he returns, a supine post-voiding film is made. If no opacification occurs, roentgenograms are taken one hour or even several hours later. In the author's experience this procedure has been helpful, not only in more promptly visualizing the obstructed ureter, but of even greater importance, in disclosing or confirming the exact site of obstruction by opacifying the ureter right down to the block.

The mechanisms whereby this procedure produces visualization of the obstructed ureter are discussed. Pre- and post-voiding films in 6 illustrative cases are reproduced to illustrate the value of the technic.

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Vesical Diverticula in Children. Alasdair MacKellar and F. Douglas Stephens. *Australian & New Zealand J. Surg.* 30: 20-31, August 1960. (Royal Children's Hospital, Melbourne, Australia)

In the years 1951 to 1958, 23 children with diverticula of the bladder were seen at the Royal Children's Hospital (Melbourne). In 13, the diverticula were associated with bladder neck or urethral obstruction; in 10 patients, however, no obstructive factor could be detected. The 10 children comprising this latter group were subjected to full routine urinary investigation, and

the findings are reported. Sex distribution was equal. Urinary tract infection was the chief presenting feature in all patients; 8 had pain on micturition; Enuresis was an incidental finding in 5 cases.

Micturition cysto-urethrography was performed, in addition to the standard radiographic procedures, in all the children in the series. It proved important not only for diagnosis but also for study of the physiological activity of the diverticula and of other parts of the urinary tract. In normal children, the bladder outline during voiding becomes finely irregular; a rounded shape is retained but the thin lateral walls may bulge, creating a trilobar outline, when viewed in the antero-posterior projection. The shape and size of diverticula were different when viewed during the resting and emptying phases of bladder activity. Small diverticula or even small inconspicuous irregularities in bladder outline ballooned into large and rounded protrusions during micturition. Two types of diverticula were identified—the localized globular pocket with narrow neck and the less common diffuse wide-necked bulge of the lateral wall of the bladder. Ureteral reflux was observed in 5 of the 10 patients and was usually unilateral. Electromanometric pressure readings of the bladder and urethra were undertaken in 4 patients, and in all the results were considered positive with respect to the presence of residual urine. On the basis of this test, it is presumed that urethral obstruction is not the cause of the formation of the diverticula.

Cystoscopic and operative findings indicated that the more common narrow-neck diverticula occur mainly in relation to the lateral cornu of the trigone, sometimes impinging on and sometimes engulfing the ureteric orifice. In the wide-neck type of diverticula, the appearance suggested a wide herniation of the lateral wall of the bladder, with the protrusion wider at its neck than at the dome. When the cystoscopic and operative findings were correlated with the radiographic features, a relationship between the location of the diverticular orifice and competence of the ureterovesical valve was established. If ureteric and diverticular orifices were closely related but separate, there was no reflux. When the ureteric orifice was contiguous with the orifice of the diverticulum, there was slight reflux and no ureteric enlargement. When the orifice of the ureter was engulfed by the diverticulum, there was free reflux and the ureter was enlarged.

Surgery was performed in 9 of the 10 children in the series. Eleven diverticula were repaired. The patients were followed for periods ranging from six months to two years; at the end of that time all were symptom-free. The degree of reflux after operation was variable, and in only 2 ureters was it corrected by surgery.

In all the cases except 1, muscle fibers were demonstrated in the wall of the diverticulum, but the amount of muscle was much less than that found in normal bladder wall. The authors therefore conclude that a defect in the muscle coat is the primary developmental anomaly and that herniation of the bladder mucosa takes place between the muscle bundles as a result of the normal bladder pressure associated with micturition both during intra-uterine life and after birth. The muscular defect also involves the terminal ureter and is responsible for the impairment of the intrinsic ureterovesical valve mechanism.

Four roentgenograms; 17 diagrams; 3 tables.

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Double-Contrast Cystography in Tumors of the Urinary Bladder. Osborne Bartley and Carl Gustaf Helander. *Acta radiol.* 54: 161-169, September 1960. (Sahlgrenska Sjukhuset, Gothenburg, Sweden)

The authors discuss their experience in the demonstration of bladder tumors by a modified double-contrast technic. After the bladder has been emptied by catheter, 8 to 10 ml. of Dionosil aqueous is injected with the patient supine. This is followed by an injection of CO₂ through the catheter until the patient experiences a desire to empty the bladder, generally when 200 to 300 ml. of gas has been introduced. The opaque contrast medium forms a coating on the mucosa which contrasts with the gas. Roentgenograms are taken with the patient both prone and supine; right and left lateral projections are also desirable. Exposure should be made with both horizontal and vertical projections in each position; oblique views are also desirable. For investigation of the base of the bladder, an axial view of the pelvis is taken perpendicular to the base of the bladder, with the patient semirecumbent and the beam vertical.

The gonadal dose does not appear to be so great as to constitute a serious contraindication to the procedure from the genetic standpoint, especially since most of the patients with bladder neoplasms are of relatively advanced age.

The authors have performed 75 double-contrast cystographic examinations, 20 of them in patients with verified bladder tumors. The double-contrast method proved definitely superior to cystography with a single contrast medium. Its value lies in the possibility of determining the relation of tumors to the base of the bladder, in permitting demarcation of even very small tumors without tangential views, and in facilitating evaluation of the degree of malignancy.

Seventeen roentgenograms; 1 drawing.

THEODORE E. KEATS, M.D.
University of Missouri

Radiographic Features of Urinary Schistosomiasis. M. Ghigo and M. Magrini. *Radiol. med.*, Milan 46: 341-354, April 1960. (In Italian) (Istituti Ospedalieri di Santa Corona in Pietraligure, Italy)

The article is based on radiologic findings in 47 patients with *Schistosoma hematobium* infestation studied in the Department of Radiology of the Royal Hospital of Hodeidah, Yemen. Ten cases are presented in detail.

The roentgen findings were as follows:

(a) Diffuse, more or less intense, non-homogeneous opacification of the wall of the bladder, which was outlined by a discrete circular calcific shadow, 1 to 3 mm. wide. This calcific line in the opinion of the authors is the summation of innumerable calcified eggs within the submucosa. Calcification in the bladder wall, which was the most frequent radiographic finding, is present only in chronic infestation. In spite of these extensive calcific deposits, the bladder conserves its elasticity and distensibility.

(b) In some cases, similar thin parallel calcific lines outlining the ureters, reaching upward for various distances. Very rarely this calcification may extend along the whole length of the ureter to the pelvic junction.

(c) Hydroureter and hydronephrosis, which occur almost constantly, appearing rather early in the course of the disease.

(d) Bladder calculi, which are a late manifestation. Although 30 per cent of the 47 patients studied had

urinary bladder calculi, their occurrence in Yemen was not uncommon in patients without bilharziasis.

Twenty-two roentgenograms.

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Suprapubic Micturition Cystography with Constant Filling in Children. J. Bryndorf, E. Rostgaard Christensen, and E. Sandøe. *Acta radiol.* 54: 204-208, September 1960. (Rigshospitalet, Copenhagen, Denmark)

A new micturition cystographic technic, of particular value in the newborn and in early infancy, is described. The patient is forced to micturate during the examination by continuous filling of the bladder with contrast medium via a suprapubic catheter.

Under local anesthesia the bladder is punctured with a cannula (external diameter 1.6 mm.), 0.5 to 1 cm. above the upper margin of the symphysis pubis in the midline. A nylon trocar is then inserted, and the cannula removed and replaced by a polyethylene catheter. A detailed description of the x-ray technic, including the projections, contrast medium, and gonad doses, is given in a previous paper (*Acta radiol.* 52: 426, 1959. *Abst. in Radiology* 75: 676, 1960). Hypaque diluted with sterile normal saline is allowed to flow into the bladder by gravity from a distance of 60 cm. above the symphysis. The infusion is stopped just before micturition is expected, and an anteroposterior roentgenogram is obtained. An interval of thirty minutes is allowed so that any delayed reflux will be demonstrated. The infusion is then resumed until the patient again voids, when as many micturition films as required, both oblique and true lateral, are exposed.

Twenty-six patients, 16 children and 10 adults, were studied by this method. The technic was found to be particularly useful in newborn and small infants, because of the excellent control of micturition. Urethral valves were demonstrated in 2 children, aged three and eighteen months. Good cystograms were also obtained in the adults and older children, but quite as satisfactory results could have been achieved with the transurethral technic. No complications in connection with the examination were encountered.

Two roentgenograms; 1 photograph.

SAMUEL B. HAVESON, M.D.
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MISCELLANEOUS

Roentgen Manifestations in Progressive Systemic Sclerosis (Diffuse Scleroderma). Bela Gondos. *Am. J. Roentgenol.* 84: 235-247, August 1960. (1720 Connecticut Ave., N. W., Washington, D. C.)

It has been recommended that the term "scleroderma" be replaced by "progressive systemic sclerosis," since scleroderma is only one of the symptoms of a disease neither solely nor primarily involving the skin. The sequence is the same in every organ: (a) edema, followed by (b) proliferation of the connective tissue and sclerosis of the collagenous bundles (induration), and finally (c) atrophy.

Experiences with 25 cases of progressive systemic sclerosis observed in the District of Columbia General Hospital during the last sixteen years are reviewed. Seventeen of this number, including one which came to autopsy, were proved histologically. In the remaining 8

patients, either no biopsy was obtained or the result of biopsy was inconclusive and the diagnosis was based upon the dermatologic manifestations. The incidence in females was more than twice as high as in males. Most of the patients (22) were between thirty and sixty years of age. Of the viscera, the gastrointestinal tract was the most commonly involved. In 8 patients there was involvement of the heart, and in 7 of the lungs. Bone changes and soft-tissue calcification were less frequent.

In "scleroderma heart disease" the heart is commonly enlarged; it generally has a triangular shape and there is diminished pulsation at fluoroscopy. The findings are similar to those in myxedema and in pericardial effusion.

Progressive systemic sclerosis tends to involve the lower lung fields and probably extends gradually in a proximal direction. A diffuse interstitial infiltration and an infiltration intermingled with small cysts may also be found. In advanced cases, pneumothorax may occur secondary to the rupture of pneumatoceles. Pleural effusion is rare. Pulmonary or pleural calcification has not previously been reported, but pleural calcification was seen in one of the author's patients who had combined silicosis and progressive systemic sclerosis.

Dilatation and decreased peristaltic activity were the most common abnormalities encountered on roentgen examination of the gastrointestinal tract. The passage of barium may be considerably delayed. The essential pathologic changes are thickening of the submucosa by increased fibrous tissue and atrophy of the muscular layer. Involvement of the esophagus may be demonstrated roentgenologically during that phase of the disease when the patient still has no clinical symptoms on which a diagnosis can be based. The wide, atonic esophagus is visualized not only by its barium content but also by air in the lumen, with barium coating the mucosa. This latter finding is due to the fact that, after the passage of the bolus, the esophagus does not contract normally. When the patient is in the horizontal position, the barium may remain in the esophagus for hours. The stomach generally exhibits no striking abnormalities, but in one of the author's cases, there was thickening and marked irregularity of the mucosal folds. In the small intestine, the changes are generally localized in the proximal portion. Involvement of the duodenum is common. This localization may be of value in differentiating progressive systemic sclerosis from the sprue syndrome. If the patient is ambulatory, there may be no significant delay in the motility of the diseased small intestine. The large bowel may show narrowings and pouch formations; an important feature is the asymmetric location of the pouches in their relationship to the haustrations.

The bones were involved in a fourth of the author's cases, usually the terminal phalanges of the fingers. The disease generally begins in the distal end of the phalanx. The first appearance of destruction may, however, occur in the middle third, resulting in separation of the distal and proximal portions of the bone. In the active phase, irregular destruction with poorly defined borders may be seen. During inactive intervals, a "reconstruction" takes place with a tendency to approximate the normal shape of the bone. This commonly results in a conical deformity, with a pointed end of the affected long bone.

Soft-tissue calcification was observed in 4 of the series.

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Thickening of the periodontal membrane, usually of the lower teeth, has been reported and is considered characteristic of the disease.

Twenty roentgenograms; 2 tables.

MICHAEL LAZOREK, M.D.
St. Vincent's Hospital, N. Y.

Familial Recurring Polyserositis. William R. Eyler, Robert K. Nixon, and Robert J. Priest. *Am. J. Roentgenol.* 84: 262-268, August 1960. (The Henry Ford Hospital, Detroit 2, Mich.)

Familial recurring polyserositis is a hereditary disorder limited almost exclusively to Armenians, Arabs, and Jews; its onset is for the most part before the third decade. The disease is found almost twice as commonly in males. Acutely painful attacks involving the abdomen, chest, or joints, and occurring in an episodic, repetitive fashion, are characteristic. In the interim between attacks, the patient is usually well. The most common manifestation is the acute abdominal attack. The pain may remain localized or spread diffusely over the abdomen in the course of an attack which rarely exceeds two or three days duration. Occurring in association with the abdominal pain, or at times as a separate event, is the second most common manifestation, namely, pleuritic chest pain. Joint symptoms are present in a variable number of patients and range from vague arthralgia to an acute arthritis.

Roentgen examination was performed in 17 of 20 patients with familial recurring polyserositis seen at The Henry Ford Hospital. Findings were for the most part nonspecific but were helpful in confirming the diagnosis. During attacks of abdominal pain, plain roentgenograms of the abdomen showed small-intestinal ileus, and a barium-meal study, carried out in 13 patients, revealed discontinuity of the barium column, dilatation, and delay in transit. During attacks of pleural pain, basilar atelectasis is generally demonstrated and pleural fluid in small to moderate amounts is often found.

Sixteen roentgenograms. ALFRED TENAGLIA, M.D.
St. Vincent's Hospital, N. Y.

Bone Formation in Laparotomy Scars. Roentgen Findings. Isadore Katz and Milton LeVine. *Am. J. Roentgenol.* 84: 248-261, August 1960. (450 Clarkson Ave., Brooklyn 3, N. Y.)

Although heterotopic bone formation in surgical abdominal scars has been known to surgeons and pathologists for many years, the shadows cast by these abnormal osseous deposits on the roentgenogram have often been erroneously interpreted. The authors report 10 cases in which bone developed in laparotomy scars and was visible on roentgenograms of the biliary tract, colon, esophagus, gastrointestinal tract, lumbar spine, or abdomen.

Many theories have been advanced to explain the formation of heterotopic bone in abdominal scars; in essence, these fall into either of two general groups: One theory is that the new bone arises from periosteum which has become detached from a neighboring bone. The second is that connective-tissue cells, under certain conditions, may undergo metaplasia and become bone-forming cells.

Heterotopic bone formation in surgical wounds usually produces no symptoms, but a patient may complain of some tenderness in the wound. On examination, a hard tender or nontender mass may be palpated. In

one series of 64 laparotomies, the incidence of bone formation was 9.4 per cent. The bone forms within weeks or a few months after operation in practically all cases but may not be discovered for several years. Histologic examination of excised specimens has invariably revealed true bone, usually of the cancellous type.

In 8 of the 10 cases reported, the roentgen images of the scar ossifications in the roentgenograms of the abdomen were readily recognizable as bone, since they showed typical cortical and medullary structure. In the 2 exceptions, the osseous tissue, lacking the distinctive appearance of bone or even of a calcific process, was indistinguishable from the opacified gallbladder. In 1 of these 2 cases, the common bile duct was simulated perfectly. In several cases the postero-anterior or antero-posterior views of the abdomen did not show the heterotopic bone at all or it was obscured because of superimposition on the vertebral bodies. It was visible, however, on oblique views and became a potential source of confusion in the interpretation of roentgenograms of the biliary tract. In 5 patients, although the heterotopic bone was visible roentgenographically, it was not identified as scar ossification for periods ranging from one month to twenty-five years. In 2 additional patients four years elapsed prior to recognition of the ossification in the scar. In the remaining 3 patients the heterotopic bone was diagnosed as such on the first postoperative roentgenogram.

Heterotopic bone formation must be differentiated from osteophytes, malformations, and traumatic bone fragments arising from the lumbar spine, from scars of the back, from calcified costal cartilage, foreign bodies in the gastrointestinal tract and, particularly, from the opacified common bile duct.

Surgical removal of the bony mass, if symptomatic, is the only known form of treatment. There appears to be no contraindication to allowing the bone to remain.

Seventeen roentgenograms; 1 photomicrograph.

MICHAEL LAZOREK, M.D.
St. Vincent's Hospital, N. Y.

Has Co-Pay Reduced Hospitalization for X-Rays? D. Alan Sampson. *Pennsylvania M. J.* 63: 1209-1210, August 1960.

The Co-Pay comprehensive subscription agreement of Philadelphia Blue Cross carries outpatient diagnostic x-ray benefits at the hospital and, by arrangement with Blue Shield, at the office of the doctor. After a year and some four months of experience with this plan, the Nov. 6, 1959, issue of *Philadelphia Medicine* carried a 5-question request for information with answers that could be checked off, space for comment, and enough background material so that the type and extent of the practice of the responding, anonymous physicians could be ascertained. The replies were sorted by an independent business organization using IBM equipment. One hundred and fifty-five physicians answered the questions. The following conclusions were reached: (1) Sixty per cent of the respondents found that the provisions for outpatient x-ray examinations had reduced hospital admissions. (2) A high percentage of subscribers believed it is neither necessary nor more convenient to undergo needed studies as bed patients. (3) Physicians in widely diversified types of practice found that patients with the new coverage were decidedly more willing to have the needed studies as outpatients than as inpatients, as formerly. (4) Some 25 per cent of the responding physicians indicated that

under the new plan some of their patients exhibited a tendency to request more diagnostic x-ray studies than were necessary. (5) Fear of "radiation hazard," with reluctance to undergo needed diagnostic roentgen studies, was taken up in Question 5. Less than a quarter of the physicians noted that this occurred frequently in their practices, about half checked off "infrequently," and the remainder noted "never."

Stratigraphic Studies of Abdominal Neoplasms with Special Reference to the Use of Transverse Axial Stratigraphy and the Technic of Pluridirectional Shading. P. de Albertis and E. Gandolfo. *Radiol. med.*, Milan 46: 321-340, April 1960. (In Italian) (University of Genoa, Italy)

The authors stress the value of multidirectional laminagraphy (transverse, frontal, and lateral) used in conjunction with air insufflation of the stomach, peritoneal cavity, and retroperitoneal space in the diagnosis of abdominal tumors. They found transverse laminagraphy especially valuable in the localization of neoplasms. The lack of distinctness of landmarks in this procedure can be overcome by the introduction of gas into the area of interest. To illustrate these points they present their findings in 8 cases, including cysts and renal tumors, a pararenal abscess, an unsuspected and nonpalpable tumor of the body and tail of the pancreas, a cavernous angioma of the liver, and retroperitoneal lymph node masses in a patient with Hodgkin's disease.

Twenty-six roentgenograms.

ALEXANDER R. MARGULIS, M.D.
Washington University, St. Louis, Mo.

TECHNIC

The Tomogram. Its Formation and Content. Paul Edholm. *Acta radiol.*, Suppl. 193, 1960. (Karolinska Sjukhuset, Stockholm, Sweden)

The purpose of the study reported here was to analyze how the information content of the tomogram is influenced by various factors, such as the shape of the tomographed body, type of tomographic motion, tomographic angle, distance between the tomographic plane and center of the body, and the absorption of the body. The author's conclusions are as follows:

"1. The greater the tomographic angle used, the greater the tomographic distortion and the poorer the contrast and the contour sharpness obtained. In the case of sufficiently small angles, the magnitude of which is determined by the shape and size of the body and by the unsharpness in the image, a 'distortion-free image' is obtained.

"2. The distortion in tomography of hollow bodies has a particularly adverse effect on contrast and contour sharpness. The deterioration becomes abrupt if the angle exceeds the inverse cosine of the ratio between the internal and external radii of the body.

"3. In circular tomography of round bodies the tomogram has the sharpest contours when the distance

between the tomographic plane and the center of the body is equal to the product of the radius of the body and the sine of the tomographic angle.

"4. In the case of organs that can be considered as approximate affine transformations of a sphere, the contour sharpness in circular tomograms is determined largely by the radius in the tomographic plane. The radius perpendicular to this plane is relatively unimportant so long as the tomographic angle is neither small nor large.

"5. Around the tomographic image of an organ a sweep image is formed. This usually cannot be perceived, but if the absorption of the organ is high, it can be seen as a halo.

"6. Areal tomography provides a better tomographic image and better diffusion of interfering detail than linear and circular tomography.

"7. Greater definition can be obtained in the tomogram by utilizing a focus the projection of which is a rectangle instead of a square."

The details of this study are highly technical and, though the investigation was performed with great care, it probably offers little useful information to the practicing radiologist. The work is highly recommended, however, to the physicist concerned with the details of diagnostic techniques and to those radiologists with a mathematical background who are interested in the principles and theories of tomography and the formation of the tomographic image.

Seventy-four figures. JOHN E. SHICK, M.D.
The Henry Ford Hospital

A Simple Device for Rapid Copying of Roentgenograms. William C. Owsley, Jr. *Texas State J. Med.* 56: 676-677, August 1960. (214 Hermann Professional Bldg., Houston 25, Texas)

The copying of roentgenographic films with the Polaroid Land camera is described. Paper prints can be made in about two minutes and finished 3 1/4 x 4-inch lantern slides can be produced in about ten.

A Polaroid No. 208 copymaker is modified by replacing its plywood base with a homemade glass-topped box that contains a circular fluorescent tube. This provides a source of transmitted light in addition to the reflected light sources furnished with the unit. The author's light box is made of 3/4-inch plywood, with outside dimensions of 7 x 21 x 22 inches. The glass portion of the top measures 14 x 17 inches. The copymaker is attached to the box with 2 screws, and the fluorescent tube is wired into the copymaker base through a toggle switch. The camera is detachable from the stand; when attached, it is automatically centered to the glass portion of the light box top.

Use of a horizontal light box eliminates the need for clips to hold the roentgenogram during exposure. The film can be moved about on the box so that any part of it is centered, giving a range from coverage of a 14 x 17-inch roentgenogram on a 3 1/4 x 4 1/4-inch print down to a 1:1 reproduction of a small area of interest.

RADIOTHERAPY

The Early Estimation of the Results of Treatment for Cancer. J. L. Haybittle. *Brit. J. Radiol.* 33: 502-507, August 1960. (Radiotherapeutic Centre, Addenbrooke's Hospital, Cambridge, England)

Methods for obtaining an early estimation of the

results of cancer treatment are discussed. At a number of sites the time taken to collect a suitable number of patients is comparable with the maximum survival time of an uncured patient. As a consequence, simple actuarial calculations can be used soon after the last

case is treated to estimate the final result. At other sites, where the survival time of some of the uncured patients is long compared with the period required to collect sufficient cases, some hypothesis is necessary about the frequency with which future deaths from cancer may occur. In a number of examples it is shown that the "Extrapolated Actuarial" method, which assumes that the probability of dying from cancer decreases exponentially with time after treatment, could have been used successfully to predict the final results of treatment provided the collection period plus the minimum follow-up time was at least seven years.

Three graphs; 3 tables.

AUTHOR'S SUMMARY

The Results of Treatment of Hypophyseal Tumors.

A Retrospective Survey. K. Decker and H. Lauter. *German M. Monthly* 5: 265-267, August 1960. (Universitäts-Nervenklinik, Munich 15, Germany)

One hundred and twenty-four patients with hypophyseal tumors were seen at the Munich University Neurological Clinic between 1946 and 1956. Diagnosis was established histologically in 80 cases either at biopsy or autopsy; in the remainder successful radiotherapy made surgery unnecessary and the diagnosis could not be confirmed. In 43 patients features of acromegaly were present. An attempt has been made to assess the role of radiotherapy and surgery in hypophyseal tumors on the basis of 103 of the patients who were treated and followed, some for as long as twenty-five years. Follow-up studies included neuropsychiatric examination, skull roentgenograms, and in many cases ophthalmological and endocrinological investigations.

Surgery was performed on 52 patients immediately upon confirmation of the clinical diagnosis. Altogether 73 operations were done on 70 patients with an operative mortality of 16.4 per cent. In 51 patients the initial treatment was irradiation; 12 of this number later underwent surgery. There was no indication that pre-operative irradiation increased the risk of operation. Details are not given, but generally roentgen therapy was administered with small-field techniques requiring careful aiming of the beam, with or without rotation. Employment of a submaxillary field proved especially useful in a few acromegalics as it provided good dosage distribution with decreased irradiation of the cranial nerves. Hormones, particularly adrenal preparations, were given in some cases.

Of the 103 patients included in the survey, 72 were alive at the time of the report. Fifty-two of these are considered cured and able to work. Thirty-one patients had died, 12 immediately after operation. In 20 patients results were not satisfactory. Inability to work was mainly the result of visual difficulties. Serious endocrinologic and mental changes occurred in many patients of both treatment groups; these are attributed to the patient's condition at the time treatment was begun rather than to its consequences.

It is concluded that either surgery or roentgen therapy will produce good results in about half the patients with hypophyseal tumor. The choice between the two depends on factors which include the acute operative risk and the assessment of potential radiation damage to normal structures. Contraindications to roentgen therapy are evidence of suprasellar damage and rapid deterioration of vision, either before treatment or during the first course of irradiation.

JAMES W. BARBER, M.D.
Cheyenne, Wyo.

Radiation Therapy of Carcinoma of the Tongue.

Erich M. Uhlmann and Marvin E. Weiner. *Surg., Gynec. & Obst.* 111: 363-370, September 1960. (Michael Reese Hospital and Medical Center, Chicago, Ill.)

The authors report on a series of 86 patients with carcinoma of the tongue, observed from 1938 to 1953, inclusive, and treated mainly or exclusively by radiant energy. The mean age of these patients was sixty-one years, with an extreme range between twenty-six and eighty-six years. In 84 patients, the histologic examination showed squamous-cell carcinoma, with varying grades of malignancy; in the other 2, an adenocarcinoma and a lympho-epithelioma were diagnosed. In 27 patients the carcinoma originated in the anterior third of the tongue, in 29 in the middle third, and in 30 in the posterior third. Only one-third of the patients with carcinoma in the anterior third of the tongue had lymph-node involvement at the initial examination; 62 per cent of the primary lesions in the middle third showed metastatic spread to the lymph nodes; metastases had developed in 70 per cent of the primary carcinomas of the posterior third. In 7 patients metastases had occurred to such distant organs as larynx, esophagus, and lungs.

Two patients refused treatment. Of the 84 who were treated, 10 received only radium implants; 8 of these had early lesions in the anterior two-thirds of the tongue without local extension or metastatic spread; 2 had posterior tumors. Fourteen of the remaining 74 patients received telecurietherapy as the only form of treatment; all had bilateral metastases to the lymph nodes of the neck when first observed, and treatments were given as a palliative measure. Fifty-six patients received combined therapy. In a few instances intra-oral roentgen therapy was added as a therapeutic measure, and 1 patient had a local surgical excision.

Twenty-four (28.5 per cent) of the treated patients were lost to follow-up. The five-year survival rate was highest in the group with primary lesions in the anterior third of the tongue (33 per cent); it was almost identical in the groups with cancers of the middle and posterior third (18.8 per cent and 20 per cent, respectively). The overall salvage rate for the 84 treated patients was 23.8 per cent. Apparently, the presence or absence of lymph-node metastases at the time of therapy is prognostically more important than the localization of the primary tumor. Of those patients who seemed to be free of metastases, 30.7 per cent lived five years without symptoms; the presence of lymph-node involvement reduced the five-year survival rate to 17 per cent. An indication of the advanced stage of the disease at the time of therapy in this group is found in the observation that, of the 84 patients treated, 15 (17.8 per cent) died within a year.

Treatment consisted of radium in the form of telecurietherapy with a 4-gram bomb and/or implantation of radium in the form of low-intensity needles. Of the patients with advanced lesions, 16 per cent were treated with telecurietherapy only. With the exception of these patients, who were treated solely for palliative purposes, the minimum amount of radiation administered was 6,000 to 7,000 gamma roentgens to the primary tumor.

The authors state that this report represents an attempt to evaluate the results of radiotherapy in the management of cancer of the tongue and to establish a base for comparison with results achieved by surgery alone. At present, the five-year survival rate after

radiation therapy ranges between 20 and 30 per cent in large centers. The fact that an operation is technically feasible is not necessarily a logical reason for choosing surgery when an alternative and less mutilating treatment is available and equally successful. It is felt that, unless the now advocated radical surgical treatment of carcinoma of the tongue shows unqualified superiority as expressed in considerably higher five-year survival figures, it should not replace radiation therapy.

One table.

H. W. SCOTT, M.D.
University of Pennsylvania

The Role of Radiation Therapy in Carcinoma of the Larynx. Joseph L. Goldman and Sidney M. Silverstone. *Ann. Otol., Rhin. & Laryng.* 69: 890-905, September 1960. (Mount Sinai Hospital, New York, N. Y.)

Almost three and a half decades of experience with radiation therapy in laryngeal cancer at the Mount Sinai Hospital (New York) has been reviewed. From 1931 to 1959, 312 cancers of the larynx and laryngopharynx were treated by irradiation. Of these, 179 were intrinsic and 133 extrinsic. Further subdivision, with five-year survival figures, is as follows (the percentages do not include patients lost to follow-up or dead from other causes):

	No. of Cases	Determinate five-year Survivals
I. Intrinsic	179	
A. Suitable for partial laryngectomy	68	30 (88%)
B. Suitable for laryngectomy	111	46 (63%)
II. Extrinsic	133	
A. Anterior group (epiglottis, false cord, upper half of aryepiglottic fold)	59	25 (56%)
B. Postero-lateral group (arytenoid, pyriform sinus, lower half of aryepiglottic fold, post-cricoid)	40	9 (32%)
C. Extensive group (both anterior and posterolateral locations involved)	34	3 (14%)

The objectives in treatment of carcinoma of the larynx and laryngopharynx are first to save life, secondly to save the larynx, and thirdly to save the voice.

The authors agree with others that the most important single factor in prognosis is involvement of the cervical lymph nodes, which is dependent chiefly on the site of the primary tumor. True cord lesions, with the least tendency to metastasize, have, of course, the best prognosis, with a determinate survival rate for either partial laryngectomy or radiotherapy of 80 to 90 per cent. The choice of procedure, therefore, is concerned with the factor of voice. In the authors' opinion there is no question but that radiation therapy yields by far the better voice.

Early in the period covered by this study, 200 to 400 kv x-ray therapy was employed; mucous membrane reactions and radiodermatitis of moderate intensity

occurred regularly but usually healed. The most troublesome complication was persistent laryngeal edema. At present, cobalt-60 teletherapy is used. No separate analysis of the results with these two modalities is given except to state that with cobalt 60 the skin manifestations are minimal and the mucous membrane reactions are slight to moderate in intensity; post-irradiation edema of the arytenoids still occurs and may produce hoarseness. Tumor doses in the range of 5,000 to 7,000 r over a period of five to eight weeks have been administered. To reduce post-irradiation edema it has been found preferable not to exceed a dose range of 5,500 to 6,000 r in five to six weeks and to keep the treatment field size to the minimum necessary for the known extent of the growth.

The authors believe that laryngectomy with radical neck dissection should be performed as a primary procedure when a small intrinsic lesion and palpable cervical lymph nodes exist. In the laryngopharynx the growths which are located anteriorly and which involve the false cords, epiglottis, or upper half of the aryepiglottic folds can be treated by either surgery or irradiation, with radical neck dissection if the lymph nodes are involved. Posterolateral laryngopharyngeal tumors are best managed by radiation therapy followed by radical surgery within three to six weeks; in this type of lesion a tumor dose of 5,500 r is delivered by radio-cobalt in five weeks. No undue interference with wound healing has been encountered.

One drawing; 10 tables. DAVID SILVER, M.D.
Los Angeles, Calif.

Treatment of Carcinoma of the Bladder: A Symposium. *Brit. J. Radiol.* 33: 471-490, August 1960.

At the British Institute of Radiology on Jan. 14, 1960, a symposium on the treatment of carcinoma of the bladder was presented, comprising four papers. Abstracts of these contributions follow.

I. Treatment by Interstitial Irradiation Using Tantalum 182 Wire. H. J. G. Bloom. *Brit. J. Radiol.* 33: 471-479, August 1960. (Royal Marsden Hospital, London, S. W. 3, England)

Bladder carcinoma forms a broad spectrum of malignant behavior. At one end of the scale there is the well differentiated papillary tumor that remains confined to the mucosa for long periods and at the other end the highly malignant solid anaplastic growth which soon infiltrates through the bladder wall into the perivesical fat and gives rise to lymphatic and blood-borne metastases.

The author is concerned here with the treatment of limited bladder cancer infiltrating no more deeply than the muscle coat; in other words, cases in which there is a real hope of cure. He contends that such cases are best treated by interstitial irradiation, for which he prefers radioactive tantalum wires. The chief advantages of tantalum wire over radioactive gold grains or radon seeds for implant therapy are: (1) greater accuracy in introducing the radioactive material into the bladder wall; (2) the ease of removal and reinsertion of the wires if at operation the original insertion is found to be unsatisfactory; (3) a considerably more uniform distribution of radiation; (4) greater control over the dose delivered, in that the sources can be removed at any desired time; (5) the relatively long half-life of tantalum 182 (one hundred and eleven days), so that wires can be held in stock and made available at short notice.

The ideal case for an implant is one in which there is a solitary tumor, not exceeding 4 cm. in diameter, with early infiltration of muscle and without obvious potential malignant changes elsewhere in the mucosa. The procedure of tantalum-wire implantation has been fully described elsewhere (Wallace *et al.* Brit. J. Radiol. 25: 421, 1952. Abst. in Radiology 60: 928, 1953). Briefly the wires are inserted during laparotomy with a special wire introducer. They are removed per urethra in the ward. The aim is to deliver between 6,000 and 6,500 r at 0.5 cm. from the plane of the implant in five to seven days. The acute irradiation reaction usually subsides in the course of three to four weeks, but occasionally lasts for two to three months.

Since 1951, approximately 250 cases of carcinoma of the bladder have been treated by tantalum wire implants at the Royal Marsden or St. Peter's and St. Paul's Hospitals (London). In 98 per cent of these the tumor was a transitional-cell carcinoma. The results were as follows, with no allowance for postoperative deaths and deaths due to other causes:

Stage	Cases	Three-year Survivals
Mucosal	86	62 (72%)
Muscular	59	29 (49%)
Total	145	91 (63%)
		Five-year Survivals
Mucosal	44	31 (70%)
Muscular	30	12 (40%)
Total	74	43 (58%)

Eleven illustrations; 6 tables.

CAPT. HARRIS W. KNUDSON, M.C.
Lackland AFB, Texas

II. Treatment by 2 MeV X Rays. Robert Cox. Brit. J. Radiol. 33: 480-483, August 1960. (Westminster Hospital, London, S. W. 1, England)

Since 1951, 102 cases of carcinoma of the bladder were treated by 2-Mev x-rays at the Westminster Hospital (London). These included all cases which could not be managed by endoscopic diathermy, fulguration, or endoscopic resection except for those patients who were moribund or had widespread metastatic disease. Twenty-six cases are available for five-year and 58 for three-year study. At first the dose rate was 200 r/day to a total of 6,000 r; later a number of patients received 300 r/day for a dose, in some instances, as high as 8,000 r. An anterior and two anterolateral ports were used in an effort to treat the whole bladder and to spare the rectum so far as possible.

Five of 8 patients (62.5 per cent) with non-infiltrating lesions were alive at the end of three years, and 19 of 50 (38 per cent) with infiltrating lesions.

Post-irradiation complications were fairly common and consisted of perineal fibrosis, "systolic" bladder, necrosis of bowel and bladder, bleeding, and gross fibrinous exudate.

The author concludes that megavoltage radiotherapy will not entirely displace previous methods of treatment, but "it forms a massive contribution to our armamentarium in the treatment of this common and serious disease."

Five tables. CAPT. HARRIS W. KNUDSON, M.D.
Lackland AFB, Texas

III. Pathological Changes in the Bladder Following Irradiation. N. F. C. Cowing. Brit. J. Radiol. 33:

484-487, August 1960. (Royal Marsden Hospital, London, S. W. 3, England)

The gross and microscopic changes found in the bladder after irradiation for cancer are described. Tissues from 50 total cystectomy specimens were available for study. Thirty-five patients had received some form of radiotherapy; 15 had received no such treatment and therefore served as "controls."

The changes observed included: (1) contraction of the bladder with thickening and fibrosis of the wall and reduction of the luminal capacity; (2) hyperemia of the mucosa, often characterized by prominent telangiectatic vessels; (3) mucosal edema, sometimes so severe as to produce an appearance of bullae (bullous edema); (4) superficial ulceration of the urothelium with patchy exudate on the surface; (5) deep ulceration extending into the submucosal and muscle layers.

Three photomicrographs.

IV. Surgery in the Treatment of Bladder Tumours. D. M. Wallace. Brit. J. Radiol. 33: 487-490, August 1960. (Royal Marsden Hospital, London, S. W. 3, England)

The role of surgery in the treatment of cancer of the bladder is discussed in general terms with respect to diagnosis, access to the tumor, salvage of patient, and palliation. The author's series comprised 100 cystectomies. In 74 of the patients radiotherapy had failed to control the tumor, which was still technically operable. In 26 cases excision was selected as the first form of therapy, either because the lesion was a pure squamous-cell carcinoma or because the patient expressed a preference for radical excision. Seven of the 15 deaths in the simple cystectomy group of 74 patients were the result of attempting emergency cystectomy for bleeding with a hemoglobin of less than 30 per cent. The deaths (48) that occurred after the patient had left the hospital were predominantly due to incomplete removal of the tumor. The mortality rate for patients undergoing the radical operation was 21 per cent. Of 64 patients available for three-year study, 24 had survived.

The author considers the scope of surgery limited but not negligible. In a series of over 2,000 cases of bladder cancer, extirpative surgery was employed in only 120 patients. While most of the patients were obviously selected as the survivors after a period of irradiation, the results are not hopeless and it behooves every radiologist to work in close association with his urological colleagues both before treatment and after.

Seven tables. CAPT. HARRIS W. KNUDSON, M.C.
Lackland AFB, Texas

The Spectra of X-Rays Scattered in Low Atomic Number Materials. W. R. Bruce and H. E. Johns. Brit. J. Radiol. Suppl. No. 9, 1960. (Ontario Cancer Institute, Toronto, Canada)

The spectra at various depths and the central axis depth dose values are presented for 50, 100, 200, 500, and 1250 Kev radiation for field sizes of 25, 50, 100, and 400 sq. cm. and for infinite fields. A combination of analytic and Monte Carlo methods is used for the calculations. These take into account photoelectric effect and Compton scattering but neglect pair production and coherent scattering.

Seventy-three diagrams and charts; 27 tables.

LUCILLE DU SAULT
The Henry Ford Hospital

RADIOISOTOPES

Cardiotoxic Thyroid and Radioactive Iodine. Everett E. Hammonds, Kenneth E. Corrigan, and Henrietta S. Hayden. *J.A.M.A.* **173**: 1902-1906, Aug. 27, 1960. (E.E.H., 280 W. Maple, Birmingham, Mich.)

An attempt was made to detect abnormalities of thyroid function, using I^{131} , in patients with heart disease who responded poorly to conventional therapy. Twenty-five of 43 patients studied were found to have an elevated intrinsic thyroid function, and in none of these had hyperthyroidism been diagnosed clinically. The thyroid was palpable and nodular in 10 patients. Five had had operations on the thyroid gland ten or more years previously. These 25 patients were given I^{131} therapy conservatively and cautiously, the idea being for the patient to end treatment with normal thyroid function rather than a state of hypothyroidism. This was accomplished and was accompanied by a satisfactory improvement in 23 patients; 2 died of myocardial infarction. Nine patients required no further treatment after the I^{131} therapy.

Two illustrations; 1 table.

WILLIAM MARTEL, M.D.
University of Michigan

Radioactive Iodine Concentration in the Fetal Human Thyroid Gland from Fall-out. William H. Beierwaltes, Horace R. Crane, Audrey Wegst, Norma R. Spafford, and Edward A. Carr, Jr. *J.A.M.A.* **173**: 1895-1902, Aug. 27, 1960. (University of Michigan Medical School, Ann Arbor, Mich.)

Twenty-seven human fetal thyroid glands from 25 pregnancies, 12 human adult thyroid glands, 25 adult and fetal hog thyroid glands, and 11 reagent blanks were analyzed for I^{131} activity from fall-out.

Radioactivity compatible with I^{131} was found in the human fetal thyroid gland. The maximum concentration of I^{131} was 265 $\mu\mu\text{c}$ per gram of fetal thyroid tissue, 29.1 $\mu\mu\text{c}$ per gram of adult hog thyroid tissue, and 22.9 $\mu\mu\text{c}$ per gram of adult thyroid tissue. The highest activity found on a reagent blank was 10.0 $\mu\mu\text{c}$. Data on fetal pathology, age of fetus, thyroid status of mother during pregnancy, and frequency of nuclear weapons testing were examined for correlation with the degree of concentration of I^{131} in fetal thyroid.

The calculated maximum total radiation dose delivered to any fetal thyroid gland was 0.47 rads. The average total dose was 0.05 rads. Extrapolations from data obtained by others from animals suggest that it is unlikely that this quantity of radiation would produce hypothyroidism or carcinoma of the thyroid.

Three figures; 1 table. WILLIAM MARTEL, M.D.
University of Michigan

Quantitative Observations with the Thyroxine Suppression Test of Thyroid Function. T. H. Oddie, F. F. Rundie, I. D. Thomas, I. Hales, and B. Catt. *J. Clin. Endocrinol.* **20**: 1146-1157, August 1960. (Royal North Shore Hospital of Sydney, Crows Nest, N. S. W., Australia)

The thyroidal I^{131} uptake rate, one hour after injection of the isotope, was measured in 450 subjects before and after the administration of L-thyroxine (the so-called suppression test) for about three weeks. In 57 thyrotoxic patients without prior medication, the uptake rate showed a small but significant mean rise after

ingestion of thyroxine. There was a small, insignificant mean rise in 51 thyrotoxic patients previously treated with antithyroid drugs after thyroxine ingestion. When submitted to the suppression test, most of the 345 euthyroid subjects exhibited a marked fall in the initially elevated thyroidal I^{131} uptake rate. There was, however, a small region of overlap between the two types of patients, amounting to about 0.7 per cent of the total euthyroid group and 7.3 per cent of the total hyperthyroid group. The assessment of patients in these overlapping regions is discussed.

Recommended steps in the diagnostic procedure are given in the following table:

Step	Test	Interpretation	Further Steps
<i>No prior antithyroid drugs</i>			
1	Thyroidal I^{131} uptake giving $*k_1 = u$	Clearly euthyroid	None
		Clearly hyperthyroid	None
		Borderline	Step 2
2	Thyroidal I^{131} uptake, while taking thyroxine, giving $k_1 = v$	$u < 1.16 v$, hyperthyroid	None
		$u > 1.48 v$, euthyroid	None
		$1.16 v < u < 1.48 v$, borderline	Reassess completely after two to three months. Use PBI as diagnostic aid
<i>Prior antithyroid drugs</i>			
1	Thyroidal I^{131} uptake, giving $k_1 = u$	Clearly euthyroid	None
		Borderline or raised	Step 2
2	Thyroidal I^{131} uptake while taking thyroxine, giving $k_1 = v$	$u < 1.16 v$, hyperthyroid	None
		$u > 1.94 v$, euthyroid	None
		$1.16 v < u < 1.94 v$, borderline	Step 3
3	Thyroidal I^{131} uptake after stopping thyroxine for three weeks, giving $k_1 = w$	$w < 1.16 v$, hyperthyroid	None
		$w > 1.48 v$, euthyroid	None
		$1.16 v < w < 1.48 v$, borderline	Reassess completely after two to three months. Use PBI as diagnostic aid

* k_1 is the short-term thyroidal I^{131} uptake rate.

[The statistical approach used in analyzing these

cases is a model of how statistics can be used to bring out the differences in a small as contrasted to a large group of cases.—S.F.T.]

Three figures; 5 tables. SYDNEY F. THOMAS, M.D.
Palo Alto, Calif.

Therapeutic Use of Radioactive Iodine in Heart Disease. Earl F. Beard, Alfred E. Leiser, Mavis P. Kelsey, Jose Mdalel, and Raymond Rose. Texas State J. Med. 56: 670-674, August 1960. (6655 Travis St., Houston 25, Texas)

Of 349 patients treated with radioactive iodine, 121 had cardiac disease (35 per cent). This latter number included 78 with thyrotoxicosis (thyrocardiacs), 40 euthyroid patients with intractable congestive failure and/or angina, and 3 euthyroid patients with intractable arrhythmia of supraventricular origin. Experience with these patients has caused the authors to reach the following conclusions:

1. Radioiodine therapy is a safe, certain, and relatively prompt method of permanently reducing thyroid function in the thyrocardiac patient. It is, therefore, the treatment of choice, if carefully administered.

2. In the euthyroid patient with intractable angina and/or congestive heart failure, therapeutic hypometabolism produced by radioiodine may be a useful adjunct in treatment. It is relatively safe if (a) I^{131} is given in small divided doses and (b) post-treatment clinical myxedema is avoided.

Post-treatment thyroid therapy must be carefully regulated. Anticoagulants should probably be administered routinely after therapy to patients with arteriosclerosis and coronary disease.

3. Certain euthyroid patients with unmanageable arrhythmias of supraventricular origin may be made more amenable to treatment after I^{131} -induced hypometabolism but usually must be kept at myxedema or near-myxedema levels. In this group radioiodine therapy seems indicated only as a last resort.

4. Careful evaluation of all patients with advanced cardiac disease is advisable to ascertain that masked hyperthyroidism is not overlooked.

Seven tables.

The Threshold Dose of P^{32} for Leukemic Cells of the Lymphocytic and Granulocytic Series. Edwin E. Osgood. Blood 16: 1104-1121, August 1960. (University of Oregon Medical School, Portland, Ore.)

An analysis of the threshold dose of P^{32} to control 201 patients with chronic lymphocytic leukemia and 100 with chronic granulocytic leukemia and of the P^{32} dose to maintain 133 patients with chronic lymphocytic leukemia for a mean period of 50.2 months and 49 with chronic granulocytic leukemia for a mean period of 33.6 months is presented. Most of the information is given in graphs and a series of tables.

All of the patients were treated by regularly spaced,

TABLES I-IV. OSGOOD: THRESHOLD DOSE OF P^{32} FOR LEUKEMIC CELLS

TABLE I: CHRONIC LYMPHOCYTIC LEUKEMIA: MC P^{32} TO CONTROL WITHIN 12 WEEKS

Category	N	Median	Log M	S.E.	S.D.	± 2 S.E. 95% Conf. Limits	± 2 S.D. 95% Range
All P^{32} treated	201	6.30	0.799	± 0.018	0.261	5.8-6.84	1.9-21.0
Initial WBC							
<15,000	40	5.60	0.748	± 0.04	0.265	4.66-6.73	1.65-19.0
15,000-40,000	67	4.86	0.687	± 0.026	0.210	4.32-5.48	1.85-12.6
40,000-100,000	44	6.50	0.813	± 0.031	0.208	5.64-7.52	2.5-17.0
>100,000	50	10.70	1.032	± 0.033	0.240	9.25-12.53	3.55-32.4

TABLE II: CHRONIC GRANULOCYTIC LEUKEMIA: MC P^{32} TO CONTROL WITHIN 12 WEEKS

Category	N	M	Log	S.E.	S.D.	95% Conf. Limits	95% Range
All	100	10.6	1.025	± 0.026	0.260	9.4-11.94	3.2-35.1
Initial WBC							
<40,000	28	6.82	0.833	± 0.028	0.150	5.98-7.75	3.41-13.6
40,000-100,000	25	9.56	0.978	± 0.047	0.234	7.66-11.8	3.24-28.0
>100,000	47	15.5	1.190	± 0.033	0.234	13.3-18.0	5.27-45.5

TABLE III: CHRONIC LYMPHOCYTIC LEUKEMIA: P^{32} /YEAR TO MAINTAIN

Category	N	Median	Log M	S.E.	S.D.	95% Conf. Limits	95% Range
P^{32} /year, all	133	7.48	0.874	± 0.029	0.335	6.55-8.55	1.6-35
Initial WBC							
<15,000	27	6.25	0.796	± 0.0655	0.341	4.62-8.45	1.3-30.0
15,000-40,000	46	5.25	0.720	± 0.04	0.320	4.37-6.31	1.2-23.0
40,000-100,000	29	9.20	0.964	± 0.0535	0.288	7.20-11.78	2.4-34.7
>100,000	31	12.3	1.090	± 0.0530	0.286	9.63-15.7	3.3-45.9

TABLE IV: CHRONIC GRANULOCYTIC LEUKEMIA: P^{32} /YEAR TO MAINTAIN

Category	N	Median	Log M	S.E.	S.D.	95% Conf. Limits	95% Range
All	49	17.0	1.230	± 0.066	0.460	12.4-23.2	2.04-141
Initial WBC							
<40,000	14	7.5	0.875	± 0.093	0.348	4.89-11.51	1.51-37.2
40,000-100,000	9	14.0	1.146	± 0.116	0.349	8.2-23.9	2.8-70.0
>100,000	26	28.0	1.447	± 0.070	0.358	20.3-38.6	5.38-145

titrated P^{32} , as previously described by the author (see Hahn: Therapeutic Use of Artificial Radioisotopes, 1956, Chapter 7). This method determines for the individual patient the fewest doses and the smallest doses which will bring the leukocyte count below 24,000 within twelve weeks and maintain the patient in ideal condition with a leukocyte count of 15,000 for the rest of his life.

It can be seen from the tables that the median dose of P^{32} to control chronic lymphocytic leukemia within twelve weeks was 6.30 millicuries and for chronic granulocytic leukemia 10.6 millicuries. The dose for maintenance of these two groups was 7.48 and 17.0 millicuries per year, respectively. It is of special interest that the dose requirement is related to the initial leukocyte count even after an interval of years.

On the basis of his observations the author has revised his original recommendations as to dosage. His present recommendations for the first intravenous dose of P^{32} for chronic lymphocytic leukemia are 1.5 mc if the leukocyte count is below 40,000, 2 mc if the leukocyte count is between 40,000 and 100,000 and 2.5 mc if the initial leukocyte count is over 100,000. The corresponding recommended initial doses for chronic granulocytic leukemias are 3 mc if the initial count is below 40,000, 4.0 mc if between 40,000 and 100,000 and 5 mc if the initial count is over 100,000. Subsequent doses must be determined by the response of that particular patient. It should be noted that for each patient there is a threshold dose of intravenous P^{32} below which no effect on the white blood count is observed.

Twenty-one figures. SYDNEY F. THOMAS, M.D.
Palo Alto, Calif.

Extended Resection of Bronchogenic Carcinoma. A Reappraisal and Suggested Plan of Management. G. H. Lawrence, J. H. Walker, and L. Pinkers. *New England J. Med.* 263: 615-620, Sept. 29, 1960. (Virginia Mason Hospital, Seattle, Wash.)

This report is concerned with the authors' experience with surgical resection and irradiation for the cure or palliation of bronchogenic carcinoma, with particular reference to the extended lesion. Two hundred cases of bronchogenic carcinoma, seen at the Mason Clinic (Seattle) from 1950 to July 1959, were reviewed. Follow-up information was complete in all but 3 of the 147 treated patients.

Preoperative evaluation of the patient with suspected bronchogenic carcinoma included roentgenography, fluoroscopy, endoscopy, spirometry when indicated, cytologic study of sputum and pleural fluid, and scalene-lymph-node biopsy. Despite attempted preoperative diagnosis, 37 per cent of all cancers were first diagnosed as thoracotomy. Although generally accepted criteria of inoperability were utilized, exploration revealed further contraindications to resection in 41 of 101 cases explored.

Adequate follow-up study on 46 receiving no specific therapy revealed that all had died, 90 per cent within twelve months of the diagnosis of bronchogenic cancer. The longest survival was twenty-two months.

Chemotherapy alone or in combination with irradiation did not prolong survival beyond that expected in the untreated group.

Resection was performed in 60 cases, with follow-up possible in 59. At the time of the report, 3 patients had lived for more than five years (six, eight, and nine

years, respectively). Eight had lived for more than a year and 10 had died after living longer than one year. The operative mortality was 11 per cent.

The authors define extended resection as removal not only of the lung but also of the recognizable gross extension to the mediastinum, heart, thoracic parietes, or trachea. It usually necessitates intrapericardial ligation of pulmonary vessels. Of 22 patients undergoing extended resection in this series, 4 died in the first month after operation. Only 5 patients survived over eight months. Two patients had survived, at the time of the report, thirty-two months and seventy-eight months, respectively. On the basis of their experience, the authors conclude that extended resection offers but little opportunity to improve five-year survival and should be reserved for the younger patient who can best tolerate it.

Since 1957, cobalt-60 therapy has been used, with radiation cure attempted in cases with medical contraindications to operability, in tumors technically unresectable because of localized regional extension, and in tumors of the superior sulcus. In such cases, a tumor dose of 6,000 rads is administered over a six-week period, with opposing anterior and posterior beams. Rotation therapy is not employed. No specific pattern has been adhered to in treating malignant pleural effusion. It has been found that irradiation of the entire hemithorax with cobalt 60 in moderate doses (1,500 to 2,000 rads at depths of 10 cm.) over three to four weeks will usually suppress fluid accumulation to the point of eliminating repeated thoracentesis; intrapleural injections of nitrogen mustard and radioactive colloidal gold or chromic phosphate are equally effective.

In 10 of 19 patients treated with radiocobalt for attempted cure, exploration but not resection was carried out; 2 patients were treated after resection; in the remaining 5 exploration was contraindicated. At the time of writing, 11 patients had lived for over a year and 9 were without apparent disease, the longest period being twenty-nine months. Of 38 patients treated palliatively, 11 had nonresectable tumors at thoracotomy and 4 had residual disease after resection; the remainder had contraindications to exploration. One patient has been lost to follow-up, 4 have lived for longer than a year, and 2 were alive at seventeen and eighteen months.

In the opinion of the authors, surgical resection is the procedure of choice when bronchogenic carcinoma is grossly confined to the lung. Except in rare circumstances lobectomy is the operation preferred in all lesions not requiring intrapericardial pneumonectomy. Cobalt-60 therapy administered in selected cases not suited for standard surgical resection provides a hopeful means of palliation and possible cure.

Four figures; 3 tables.

RAYMOND W. BRUST, JR., M.D.
Mercy Hospital, Pittsburgh, Penna.

Interstitial Irradiation of the Pituitary. Gordon S. Ramsay. *Proc. Roy. Soc. Med.* 53: 641-644, August 1960. (Royal Marsden Hospital, London, England)

This paper is a report on 100 patients with metastatic carcinoma of the breast who were treated by radioactive implants into the pituitary between February 1955 and March 1958. Gold was used in 54 cases and yttrium in 36. First one and later the other isotope were implanted in the remaining 10. The operation was carried out under antibiotic cover and, except for some

early cases, 50 mg. of cortisone daily was given, beginning on the day before operation, to those patients not already receiving it. In most instances the disease was far advanced and other treatment had failed. It was desired to test Y^{90} , as its half-life is for all practical purposes the same as that of Au^{198} but its isodose curves show much more rapid fall-off with distance.

Two patients were alive at the time of this report. Eleven treated with Au^{198} and 1 with Y^{90} had objective evidence of regression and 1 of these was living forty-four months after implantation. For the remainder the average survival was 19.4 months: 65 were dead in six months and 13 lived less than a month.

The extent of destruction of the pituitary was estimated in 39 specimens obtained at autopsy. In 4 the gland was totally destroyed—in 3 by Y^{90} (11.9, 12.8, and 8.6 mc) and in 1 by Au^{198} (80 mc); in 7 the destruction was estimated to be between 90 and 95 per cent and the activity of the rods ranged from 34 to 115 mc of gold and from 5.4 to 11.7 mc of yttrium. The smallest amount of Y^{90} known to have destroyed the pituitary was 8.6 mc and the largest amount proved not to have destroyed all the gland was 11.7 mc. Gold is not efficient in producing total necrosis, and in 1 case 125 mc left between 10 and 20 per cent of apparently viable cells. In 2 of the 12 cases showing objective regression, destruction was 100 per cent in 1 and 95 per cent in the other and the gonadotrophin levels in both fell to zero.

There was a high incidence of complications: headache; diabetes insipidus seen quite often in the early postoperative period but lasting only a short time in most cases; bleeding; optic atrophy; meningitis. Cerebrospinal fluid rhinorrhea and meningitis, either separately or together, occurred in 21 patients: in 10 the rhinorrhea ceased spontaneously, in 5 rhinorrhea was followed by meningitis and death. There were 5 deaths among patients in whom meningitis developed without previous rhinorrhea. A striking feature was the variation in the lapse of time between implantation of the isotope and the appearance of the meningitis.

In assessing the results in the first 100 cases, the author concludes:

1. The superiority of yttrium over gold is doubtful because all but 1 of the 12 patients showing objective regression were implanted with gold and the incidence of rhinorrhea and meningitis was lower in the gold series.

2. The transnasal approach, developed at the Royal Marsden Hospital in 1956, is not ideal. The only safe place to implant rods is low down near the floor of the fossa, and the logical approach is a horizontal one. This approach is impossible *via* the nose in many cases and septal deviation and enlarged turbinates add to the difficulties of the operation. On the other hand, the transethmoidal route permits a horizontal approach to the fossa to be made in all cases and anatomical variations do not deflect the cannula. It also appears, theoretically at least, to be a more sterile route.

Finally, it is doubtful whether complete histologic destruction of the pituitary is necessary to induce a remission.

Three figures.

Radioisotopic Study of Anemia in Chronic Renal Disease. Patrick A. Ragen, Albert B. Hagedorn, and Charles A. Owen, Jr. *Arch. Int. Med.* 105: 518-523, April 1960. (The Mayo Clinic, Rochester, Minn.)

The biologic half-life of erythrocytes labeled with

radiochromium (Cr^{51}) was determined in 16 patients with chronic renal disease. Results were normal in 14; in 2 with apparently decreased survival of circulating erythrocytes complicating factors made interpretation difficult.

Six of 8 patients with chronic renal disease had an increased rate of turnover of plasma iron based on studies using Fe^{59} . None, however, had an accelerated rate of incorporation of Fe^{59} into the circulating erythrocytes; the proportion of the dose appearing in circulating erythrocytes was normal in 2 patients and decreased in 3 others. The dichotomy between the exaggerated turnover of plasma iron and the efficiency of utilization of the iron by the bone marrow suggests an inadequate response of the marrow to the bodily need for erythrocytes.

The urinary excretion of Cr^{51} was significantly increased in a patient who had hemolytic anemia as compared with that in 2 patients with normal survival of labeled erythrocytes. The possibility that measurement of urinary Cr^{51} might be a practical alternative to assays of blood Cr^{51} in the evaluation of hemolytic disease is suggested.

One graph; 3 tables.

A Radioautographic Study of a Human Brain and Glioblastoma Multiforme After the In Vivo Uptake of Tritiated Thymidine. H. A. Johnson, W. E. Haymaker, J. R. Rubini, T. M. Fliedner, V. P. Bond, E. P. Cronkite, and W. L. Hughes. *Cancer* 13: 636-642, May-June 1960. (Medical Research Center, Brookhaven National Laboratory, Upton, N. Y.)

The radioautographic findings in a human brain and glioblastoma multiforme after *in vivo* labeling with tritiated thymidine are described. The labeled nucleoside was readily incorporated into neoplastic cells. The generation time (doubling time) of the neoplasm has been estimated from the percentage labeling. The cancer cells were apparently dividing much more slowly than were cells in several non-neoplastic populations.

Nine figures; 1 table.

AUTHORS' SUMMARY

Coronary Blood Flow Measured by a Surface Counting Technique. David D. Snyder, G. Sevelius, P. C. Johnson, and Gilbert S. Campbell. *Surg., Gynec. & Obst.* 111: 371-375, September 1960. (University of Oklahoma School of Medicine, Oklahoma City, Okla.)

In studies of cardiac output in dogs by a surface counting technic (using radioactive Diodrast) the time-activity curve registered precordially was seen to be composed of three separate peaks. The first two of these peaks represent the passage of the radioactive bolus through the right and left chambers of the heart. There was, however, some question about the meaning of the third peak, which appears simultaneously with the appearance of the radioactivity in the circulation of the neck. It was originally thought that it represented the peripheral circulation in the heart region and that the coronary circulation constituted a major portion of it. It was also considered possible that the third peak might portray the return of a portion of the tracer bolus to the right chambers of the heart *via* the coronary circulation. To answer some of the questions as to the meaning of the third peak, experiments were performed in dogs with the tracer bolus temporarily excluded from the coronary circulation. In addition, records obtained from patients free of cardiovascular disease were reviewed in order to determine the mean time for the

radioactive bolus to reach the coronary circulation and also the mean transit time of the bolus through the coronary circulation. The authors now believe that the third peak represents coronary capillary flow and not the first recirculation, because its appearance is simultaneous with the appearance of radioactivity in other nearby peripheral circulations, *i.e.*, neck muscles or kidney. On the average, the peak ends before the beginning of the earliest recirculation of the tracer bolus.

Four figures.

ROGER MALTAIS, M.D.
University of Pennsylvania

Localization of Radio-active Implants with Image Intensification and Television. J. J. Stevenson. *Proc. Roy. Soc. Med.* 53: 644-645, August 1960. (Royal Marsden Hospital, London, England)

During the five years previous to this report, implantation of the pituitary gland with radioactive material was done in more than 200 patients. At the beginning, fluoroscopy in two planes was used to localize the introducing needle and subsequent implant. With this method, however, it was impossible to perceive adequate detail, and the use of subdued

room lighting with intermittent total darkness handicapped the surgeons and anesthetists. An image intensifier was then employed: an electron optical tube consisting of 2 fluorescent screens with a high potential difference between them. When roentgen rays strike the front screen it fluoresces in the normal manner and electrons are emitted from its posterior surface in direct proportion to the amount of fluorescence immediately in front. These particles, being negatively charged, are accelerated across to the anode end of the tube and are focused on the smaller screen at the rear. Owing to the difference in the areas of the two screens and the impact with which the electrons strike the smaller, its brightness is several hundred times greater than that of the larger screen. With the aid of a simple optical attachment smaller amounts of x-rays enable the observer to see much more detail, and to see it in fully lighted rooms.

Perhaps the greatest drawback of the intensifier was the difficulty associated with the rather awkward viewing attachment. This problem was solved by the use of an industrial television chain in conjunction with the image amplifier.

One photograph.

RADIATION EFFECTS

Irradiation Damage to the Bowel. C. I. Cooling. *Proc. Roy. Soc. Med.* 53: 650-652, August 1960. (London, England)

The usual cause of irradiation damage to the bowel is radiotherapy of cervical carcinoma. The late reactions are more sinister than the early ones and occur a few months or, occasionally, years after treatment. These may be divided into intrinsic reactions, or localized radionecrosis affecting only the bowel wall, and extrinsic reactions with the indurated bowel lying in a pelvis full of fibrous tissue. The crux of the problem is the similarity of the irradiation damage to recurrent carcinoma in the pelvis. It is important to pursue the diagnosis and not abandon a case as one of hopeless pelvic recurrence when in fact the patient is tumor free. Neither should further palliative irradiation be recommended for what is already a case of over-irradiation.

Reference is made to 8 cases with the salient features given in abbreviated reports.

Two roentgenograms.

Radiation Dose in Cinecystourethrography of the Female. E. J. Pick, R. Davis, and A. J. Stacey. *Brit. J. Radiol.* 33: 451-454, July 1960. (University of London, 10 Henrietta St., London, W. C. 2, England)

The object of the investigation reported in this article was to measure the skin dose-rates delivered with varying radiographic exposures and to calculate the total individual skin doses received by a representative group of females during micrurating cinecystourethrography. From these measurements, the gonadal doses were estimated by comparison with those measured in a phantom. The extent to which various factors contributed to the total doses was analyzed.

The bladder and urethra were observed and filmed through a 35-mm. Arriflex cinecamera, mounted on a 5-in. Philips image intensifier. The film speed was 16 frames per second; Ilford HPS film was used for all examinations. Both filling and emptying of the bladder were studied fluoroscopically, and cinefilm was taken to record the most relevant observations. The x-ray unit

employed for these examinations used the General Heliphos generator Type R353, which is fully rectified, with the Mullard MRO X-ray tube Type MX204. The dose-rates were measured with a cylindrical ionization chamber, 3.6 cm. in diameter and 5.5 cm. in length, and a portable electrometer detector.

The results show that the radiation doses to the skin of the patient during micrurating cystourethrography are high. Due to the nature of the examination, the gonads inevitably receive a considerable dose. The high tube currents necessary for cineradiography involve a far greater dose-rate than those in the fluoroscopic range. In most examinations the greater part of the total dose was indeed received during cineradiography. It is therefore essential to strictly limit the time of filming.

Careful selection of exposure factors can also contribute to a reduction of dose. The combination of higher kilovoltage with a low tube current will result in a lower dose to the patient than that produced by a lower kilovoltage and a high tube current. The use of a minimum tube current at all times is essential.

Even when all these precautions are strictly observed, the doses delivered are of considerable magnitude. In addition, these patients have often had previous diagnostic studies. Hence, in children and young adults, the indication for the examination must be considered with great care and the radiation risk weighed against the expected clinical benefit.

Two illustrations; 1 table.

PETER TORREY, M.D.
University of Washington

On Multiple Myeloma Among X-Ray Personnel. S. A. Reinberg. *M. Radiol., Moscow* 5: 7-9, August 1961. (In Russian)

Three cases of multiple myeloma among x-ray personnel are reported.

The first patient, a diagnostic radiologist for thirteen years, had habitually failed to use lead gloves or other protection. The second, also a physician, had been in

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radiology for sixteen years but had been working in medical administration for four years thereafter. The third patient had been an x-ray technician for thirty years, during which time he had disregarded protective measures. The diagnoses were all confirmed by autopsy.

Since myeloma is a rare disease, it is not possible to draw statistical conclusions, but the occurrence of 3 cases in x-ray personnel out of 68 cases known to the author is at least thought-provoking.

FRANK A. RIEBEL, M.D.
Columbus, Ohio

Radiation Dose to the Skin in Roentgen Diagnostic Procedures: Optimum kvp. and Tissue Measurement Techniques. Aaron P. Sanders, Kathryn Sharpe, John B. Cahoon, Robert J. Reeves, Joseph K. Isley, and George J. Baylin. *Am. J. Roentgenol.* 84: 359-368, August 1960. (Duke Hospital, Durham, N. C.)

The authors have measured the radiation doses received by the skin during various routine roentgen diagnostic procedures, with correct and incorrect filtration. In one table is given the radiation dose for the optimum kilovoltage technic as developed by Fuchs (*X-Ray Technician* 22: 62, 1950). A second table gives the radiation dose for the tissue measurement technic. The optimum kilovoltage technic may also be referred to as the long-scale contrast technic and the tissue measurement technic as the short-scale contrast technic. In general, the Fuchs technic provides a greater latitude in the roentgenogram for deviations in procedure. In both tables, the radiation doses received during each diagnostic procedure, by small, medium, and large-size patients, are listed for exposures with inherent filtration only, and with 1 mm. Al, 2 mm. Al, and 3 mm. Al added filtration.

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A New Method for the Determination of the Instant Effect of Roentgen Rays. R. Schuppli and H. H. Wagener. *Strahlentherapie* 112: 561-566, August 1960. (In German) (Dermatologische Universitätsklinik Basel, Switzerland)

Various methods have been used to establish the biological effects of x-rays, but most of these require a relatively long period between the irradiation and the time when the different effects are recognized. A few methods, however, have been worked out to provide an immediate indication of the effect of x-rays on the biological object. The most useful appears to be pressure measurements in the skin which has been injected with saline under a constant pressure. Another method is based on the measurement of the mechanical resonance frequency of the skin by electrical techniques.

The authors measured the frequency conductivity of the skin of rabbits. An electrical oscillator was used at frequencies between 170 and 230 cycles per second. A depilated skin fold was placed over the end of an x-ray cone and two electrodes were brought in contact with the skin. By varying the oscillator frequency, two peaks of conductivity were observed, one at about 200 and the other at about 490 cycles per second. The measurements were made at the lower resonance frequency (200 c/s).

When the skin was irradiated with doses of 200 to 2,000 r, a relatively instantaneous decrease of the oscillator current occurred. (The measurements were made at voltages of 55 and 100 kv.) However, with

fractionated irradiations (with lapses of two to seven minutes), the current decrease was smaller with each succeeding exposure. When a second dose of 2,000 r was administered within seven minutes of the first, no measurable effect was noted.

A further investigation was made to determine if the measured decrease of the current occurred at all frequencies or if it was rather caused by a shift of the resonance peaks. It was proved that the decrease was caused by a shift to the right of the resonance peak at about 200 cycles per second. The authors did not attempt at this time to give a quantitative interpretation of the results.

Eight graphs. WALTER MAUDERLI, D.Sc.
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Unusual Clinicopathological Syndromes with Kaposi's Visceral and Related Sarcomata. Report of Three Cases, One Associated with Thorium Dioxide Administration. Henry T. Perkins, Jr., John V. Verner, Jr., Tatsuo Yoneyama, and E. Harvey Estes, Jr. *Arch. Int. Med.* 105: 733-745, May 1960. (University of Florida College of Medicine, Gainesville, Fla.)

Three cases are reported in which widespread vascular tumors were found at autopsy to explain the unusual clinical syndromes preceding death. Histologic examination showed the tumors to be similar to those termed Kaposi's visceral sarcoma. Of interest to the radiologist is the fact that one patient, eighteen years prior to death, had had a thorium dioxide study of the liver; a definite relationship was demonstrated between the sites of tumor involvement and the still radioactive thorium deposits.

Nine illustrations, including 1 roentgenogram.

Radiation Dosimetry in Hiroshima and Nagasaki Atomic-Bomb Survivors. E. T. Arakawa. *New England J. Med.* 263: 488-493, Sept. 8, 1960. (Oak Ridge National Laboratory, Oak Ridge, Tenn.)

Since 1956, an investigation has been under way to determine the type and total dose of irradiation received by individual survivors of the atomic bombings of Hiroshima and Nagasaki. As the bombs actually employed were not monitored for their radiation potential, the radiation delivered has been estimated from similar weapons.

When a uranium or plutonium nucleus is invaded by a neutron, the nucleus splits into two or more particles, with the liberation of a large amount of energy. This is accompanied by a marked increase of temperature, which produces extremely hot gases that move outward with great force. Fifty per cent of the total energy is released in this manner, 35 per cent as thermal radiation and 10 per cent as residual nuclear radiation; only 5 per cent is released during the first minute as initial nuclear radiation. The initial nuclear radiation consists of alpha, beta, and gamma rays in addition to neutrons. The gamma rays and neutrons are of chief concern in assays of the direct radiation effects of atomic weapons.

The direct gamma and neutron radiation emanations at Hiroshima and Nagasaki have been estimated by York (*Health Physics* 1: 390, 1959). The dose decreases in a near logarithmic fashion as the distance from the hypocenter increases. The relative gamma and neutron doses vary independently, depending on the type of bomb, but the Nagasaki bomb apparently released very little neutron energy as compared to the

Hiroshima bomb. The local fall-out occurred in both cities at about 3 km. from the hypocenter. The external integrated gamma dose from the radioactive fission products probably amounted to several rads in Hiroshima and about 100 rads in the Nishiyama area of Nagasaki. These figures are based on conditions of continuous residence without shielding and therefore represent the upper limits of doses to which residents of these areas could have been exposed. The radiation in the hypocenter areas was very weak when measured several weeks after the detonations, due to the short half-life of Na^{24} and of Mn^{56} . The integrated dose from the time of the burst to infinite time could have amounted to 100 rads in Hiroshima and 50 rads in Nagasaki.

The isodose curves of the hypocenter area demonstrated a progressive and symmetrical decrease out from the hypocenter. The intensity of the hypocenter isodose curve for Nagasaki seemed very similar to that of Hiroshima, despite the fact that York's direct dose calculations show the neutron dose in Nagasaki to be six times less than that in Hiroshima. The results of measurements in both cities on the radioactive P^{32} produced in human bones from the reaction $\text{P}^{31}(n, \gamma)\text{P}^{32}$ also show that the neutron fluxes in the two cities were approximately equal. This discrepancy remains unexplained.

Eight thousand survivors in Hiroshima and 5,700 in Nagasaki were questioned concerning their distance from the hypocenter (from which the air dose may be derived) and their shielding by surrounding structures, which are of importance in calculating the attenuation of the radiation. It was found that attenuation within a house was independent of its orientation with respect to the burst point. The protection afforded by the Japanese-type house was of limited value against ionizing radiation.

It is hoped that the studies being carried out in Hiroshima and Nagasaki, which apparently received widely different neutron doses, will shed some light upon the values of relative biologic effectiveness for human beings.

Eleven figures.

HANS A. LINDT, M.D.

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Delayed Radiation Effects in Survivors of the Atomic Bombings. A Summary of the Findings of the Atomic Bomb Casualty Commission, 1947-1959. J. W. Hollingsworth. *New England J. Med.* 263: 481-487, Sept. 8, 1960. (Yale University School of Medicine, New Haven, Conn.)

The author summarizes the findings of the Atomic Bomb Casualty Commission, 1947-59, on delayed radiation effects in survivors of the atomic bombings of Hiroshima and Nagasaki. The calculated air-dose curves for both neutron and gamma rays are available, although their range of possible error is relatively large. There was probably no significant "fall-out" and also little neutron-induced radioactivity. From the air-dose curves, it is evident that irradiation was intense (perhaps 400-800 rads) in the group exposed under 1,000 meters from the hypocenter, and that little irradiation was received by those beyond 2,000 meters (perhaps less than 20 rads). Acute symptoms occurred almost entirely in those exposed at less than 2,000 meters. Survivors under 1,000 meters were quite few and were mostly shielded heavily. The surviving population represents a group of about 60,000 persons, living

in the cities in 1950, who received definite irradiation (under 2,000 meters from the hypocenter). Of these survivors, approximately 7,000 who had experienced major acute radiation symptoms were available in 1950.

Genetic changes have been extensively investigated. Of marked importance is the fact that there were no excess of major congenital abnormalities, significant increase in stillbirths, difference in birth weights, or excessive infant mortality in the offspring of exposed parents when either (or both) was exposed under 2,000 meters from the hypocenter. (This does not apply to infants irradiated *in utero*.) A single positive finding indicative of genetic effects fitted the hypothesis that irradiation does induce sex-linked lethal mutations altering the sex-ratio at birth.

Lenticular disease, due to the bombing, was infrequent and mostly mild. Posterior subcapsular plaques were found to be strongly related to the degree of epilation, suggesting a relation to radiation dose.

The incidence of leukemia of all types was observed to be rising in 1948 and reached a peak in 1950-52. The degree of risk was clearly related to the distance from the hypocenter. The incidence of leukemia in survivors under 1,000 meters may be increased ten to fifty times. The number of cases at Hiroshima exceed threefold the cases expected in the entire anticipated lifespan of an unexposed sample of similar age and sex composition. Chronic granulocytic leukemia showed a proportionately greater increase than any other type. As the general incidence of leukemia has waned in recent years, so also has the relative prominence of chronic granulocytic leukemia as compared to the acute forms of the disease. The mechanism of radiogenic leukemia has not been elucidated; it is postulated that irradiation induces a change in nuclear gene material, leading to the so-called somatic mutation.

The survivors exposed under 1,500 meters from the hypocenter were found to have a tumor incidence twice as high as those of a control population. It seems statistically probable that the incidence of carcinoma of lung, stomach, breast, ovary, and cervix was greater in the irradiated group.

In surviving children, exposed *in utero*, microcephaly, frequently associated with mental retardation, was a regular feature of a large radiation dose delivered to the fetus of less than four months gestation.

Growth and development of children, aging acceleration, and general medical effects in adults have also been investigated.

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A Trial of Cystamine in Radiation Sickness. J. B. Healy. *Brit. J. Radiol.* 33: 512-514, August 1960. (St. Luke's Hospital, Rathgar, Dublin, Eire)

An attempt was made to assess the problem posed by radiation sickness in a women's radiotherapy ward with 27 beds. Most of the patients were receiving irradiation to large volumes of tissue (45 per cent to the thorax, 30 per cent to the pelvis, and 10 per cent to the epigastric region). In one group of 60 patients, cystamine, pyridoxin, and a control pill were used; in a second group of 52 patients cystamine and lactose were given. When the results for the two groups were taken together, no advantage could be found for using cystamine. Pyridoxin proved no better than control tablets. Lactose was as effective as cystamine. Half of the patients were apparently relieved by inert tablets.

July 1961

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